CHAPTER 16

HEMATOLOGIC ASSESSMENT

INTRODUCTION

Background

Experiments in laboratory animals have demonstrated that 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, or dioxin) is directly toxic to the hematopoietic system in several species. In one study, TCDD administered in low doses to monkeys resulted in elevated neutrophil counts while higher doses were associated with lympho- and thrombocytopenia (1). A decrease in overall cellularity and an increase in the myeloid-erythroid ratio were noted in approximately half of the sternal bone marrow samples examined at the conclusion of the experiment.

Other animal studies have shown that the toxic effects of TCDD on the hematopoietic system vary depending on the dose employed and the species examined. In many reports, it is difficult to distinguish primary effects from those occurring secondary to systemic toxicity. One study in rats using gavage doses of TCDD varying from 0.001 to 1.0 μg/kg noted depressed red blood cell counts and packed cell volumes in the high-dose group (2). In another rat experiment, elevated erythrocyte, reticulocyte, and neutrophil counts were noted with reduction in mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), platelet counts, and clot retraction times—effects that the authors felt could be attributed to systemic toxicity with terminal dehydration (3). In another multispecies study, mice and guinea pigs were found to have dose-dependent reductions in leukocytes with relative lymphocytopenia within 1 week of TCDD administration while thrombocytopenia and hemoconcentration were found in rats (4).

More recent animal research relevant to the hematopoietic system has focused on the altered cellular differentiation associated with TCDD toxicity. In mice, progenitor cells were suppressed following exposure to TCDD in doses as low as 1.0 μg/kg of body weight, and in vitro studies demonstrated that myelotoxicity occurs by a direct inhibition of proliferating stem cells (5). A subsequent study from the same laboratory demonstrated a direct effect of TCDD on cultured lymphocytes resulting in a selective inhibition of B-cell differentiation into antibody-secretive cells (6). In these and other studies (7), the authors cite evidence for the role of the aryl hydrocarbon (Ah) receptor in mediating these myelo- and lymphotoxic effects. In another report, the presence of the Ah receptor was defined in the spleens of numerous primate species (8). Though Ah receptors have been isolated in the tissue of several human organs (9-14), the relevance of these observations to dioxin toxicity remains to be proven (15).

In general, human observational studies have shown fewer and less consistent hematologic findings than the structured animal experiments. A case report of dichlorophenoxyacetic acid (2,4-D) intoxication with marked neurological findings described transient bone marrow depression with peripheral leukopenia and granulocytopenia (16). In two industrial accidents involving significant contamination with TCDD associated with

chloracne, temporary depression of peripheral leukocyte and lymphocyte formation was observed (17,18).

Several human morbidity studies have included routine, complete blood counts in examination protocols (19,20). A clinical epidemiologic study was conducted 30 years after the Nitro, West Virginia, tricholrophenol explosion. The study compared 204 highly exposed employees (86% of whom had developed chloracne) with 163 employees who were not exposed (20). No significant differences were found in the standard hematologic indices.

Numerous studies have been conducted on cohorts exposed to TCDD by environmental contamination of the soil in the Quail Run (21-23) and Times Beach (24) residential areas of Missouri. With one exception, no differences were found in any of the hematologic parameters examined. In the Times Beach study, a statistically significant increase in the mean platelet count was noted in the exposed cohort relative to the unexposed, but the difference (281,927/mm^3 vs. 249,061/mm^3) was not clinically significant. A more recent study, the first to report clinical indices in relation to tissue levels of dioxin (25), found no abnormalities in the complete blood count related to the body burden of TCDD.

In previous reports of the Air Force Health Study (AFHS) (26-28), Ranch Hand participants were found to have slightly higher mean platelet counts than Comparisons and, in the 1987 followup examination (28), a significantly greater percentage of abnormally high platelet counts as well. In the most recent serum dioxin analysis of the 1987 followup examination (29), Ranch Hands with the highest current serum dioxin levels had higher mean platelet and total white blood cell counts (WBC) than Comparisons with background levels of dioxin. Though the differences in the means between the cohorts (270,050/mm^3 vs. 259,010/mm^3 for platelets and 7,124/mm^3 vs. 6,668/mm^3 for WBCs) cannot be considered clinically significant, these results are consistent with a dose-response effect and, along with the elevation in the erythrocyte sedimentation rate (see Chapter 9, General Health), raise the possibility of a chronic inflammatory response associated with dioxin exposure.

Summary of Previous Analyses of the Air Force Health Study

1982 Baseline Study Summary Results

The functional integrity of the hematopoietic system was assessed at the Baseline examination by the measurement of eight peripheral blood variables: red blood cell (RBC) count, WBC, hemoglobin, hematocrit, MCV, MCH, mean corpuscular hemoglobin concentration (MCHC), and platelet count. These variables were analyzed in the discrete form to detect differences in the percentages of values outside the designed laboratory range, as well as analyzed in the continuous form to detect shifts in mean values between the Ranch Hand and Comparison groups.

The Ranch Hand group had a significantly higher adjusted mean MCV and MCH than the Comparison group ($p=0.05$ and $p=0.04$ respectively), although the magnitude of the difference was small in each case. The Ranch Hand adjusted mean values for six other parameters (i.e., RBC, WBC, hemoglobin, hematocrit, MCHC, and platelet count) were nearly identical to the adjusted mean values of the Comparison group, and all were well

within normal range. The percent of abnormal values for these eight variables, as established by the upper and lower limits of normal, did not differ significantly between the two groups.

The 1982 report concluded that the overall statistical findings were generally consistent, and that adverse health effects related to herbicides were not present.

1985 Followup Study Summary Results

The same eight peripheral blood variables (i.e., RBC, WBC, hemoglobin, hematocrit, MCV, MCH, MCHC, and platelet count) were analyzed in the 1985 followup. The unadjusted discrete analysis of the percent abnormal values, both low and high, showed no statistically significant difference between the Ranch Hand and Comparison groups for any of the hematologic variables. Similarly, in the adjusted discrete analyses, none of the adjusted relative risks was significant.

As no subgroup demonstrated consistent patterns of hematologic impairment, biologic relevance was not assigned to the interactions. The significant group differences found for MCV and MCH at the Baseline examination were not present in the 1985 followup analyses. The covariate effects of age, race, occupation, and lifetime smoking history were highly significant for many of the hematologic variables.

The longitudinal analyses of MCV, MCH, and platelet count found a significant difference for platelet count, with the Ranch Hands having an average decrease in platelet count between examinations and the Comparisons having an average increase. As a result, the Baseline group difference (nonsignificant) in mean values closed to near equivalence at the followup examination.

In conclusion, none of the eight hematologic variables was found to differ significantly between the Ranch Hand and Comparison groups. The expected effects of age, race, and smoking were demonstrated with most of the hematologic variables. The longitudinal analyses also suggested that neither group manifested an impairment of the hematopoietic system. Exposure index analyses did not support a plausible dose-response relationship for any of the hematologic variables.

1987 Followup Study Summary Results

The hematologic status of the Ranch Hand and Comparison groups was assessed by the examination of the same eight variables used in the two previous examinations: RBC, WBC, hemoglobin, hematocrit, MCV, MCH, MCHC, and platelet count. There were no statistically significant differences between the Ranch Hand and Comparison groups for RBC count, hemoglobin, hematocrit, MCV, MCH, and MCHC, in analyses either unadjusted or adjusted for the covariates of age, race, occupation, current cigarette smoking, and lifetime cigarette smoking history. For WBC count, the mean level was significantly greater in Ranch Hands than in Comparisons. The difference was not statistically significant after adjustment for covariates, nor were significant differences detected in the percentage of individuals with abnormal values.

Mean platelet counts also were significantly greater in Ranch Hands than in Comparisons, as was the percentage of individuals with abnormally high platelet counts. While these differences remained significant after adjustment for covariates, no platelet count was above 595,000/mm^3. Longitudinal analyses detected a significantly greater decrease in the mean platelet count in Ranch Hands than in Comparisons, despite the higher overall mean count, from the Baseline examination to the 1987 followup examination.

Serum Dioxin Analysis of 1987 Followup Study Summary Results

Several variables showed an association with initial dioxin in the unadjusted model, but when the model was adjusted for covariates, the associations became nonsignificant. Hemoglobin and hematocrit were positively associated with current dioxin when time since duty in Southeast Asia (SEA) was no more than 18.6 years and negatively associated with current dioxin when time since duty in SEA was greater than 18.6 years. For the discrete RBC count analysis, the risk of an abnormally low count was less than 1 when time since duty in SEA did not exceed 18.6 years and was greater than 1 when time since duty in SEA was more than 18.6 years. Since a low RBC count was considered abnormal for the purpose of these statistical analyses, the trend in relation to current dioxin was similar to that in the continuous analyses of hemoglobin and hematocrit. In the discrete analysis of prothrombin time, the trend in relation to current dioxin also was similar to that in the continuous analyses of hemoglobin and hematocrit. In the categorized current dioxin analyses, whenever the overall contrast showed significant, or marginally significant, differences among the categories, the mean level or percent abnormal in the three categories of Ranch Hands (i.e., officers, enlisted flyers, and enlisted groundcrew) tended to exceed the corresponding mean level or percent abnormal in the background category that consisted of Comparisons.

The longitudinal analyses of MCV, MCH, and platelet count displayed no significant associations with dioxin.

In summary, the results of the previous analysis reveal no evidence for hematopoietic toxicity secondary to dioxin exposure. Statistical analyses of two variables (WBC and platelet count) raised the possibility of subtle biologic effects that cannot be considered clinically significant but do point to the need for followup in future examination cycles. The increased platelet and WBC counts, in addition to the elevation of erythrocyte sedimentation rates (in the general health assessment) may indicate the presence of a chronic inflammatory response to dioxin exposure.

Parameters for the Hematologic Assessment

Dependent Variables

The analysis of the hematologic assessment consisted of data from the laboratory examination only. No questionnaire or physical examination data were analyzed as part of the hematologic assessment.

Laboratory Examination Data

A total of 13 hematology variables were measured at the laboratory as part of the 1992 followup examination and analyzed statistically. These variables include 5 cell counts, 1 RBC cell morphology, 6 measures of absolute blood counts, and a coagulation measure (prothrombin time). These variables were determined by routine hematologic procedures. In particular, the cell count indices were performed on the Coulter S Plus® automated instrument, and prothrombin time was measured on the MLA Electra 1000-C® instrument. All dependent variables were analyzed in the continuous form, except for the RBC morphology. RBC count, WBC count, hemoglobin, hematocrit, platelet count, prothrombin time, and the RBC morphology also were analyzed in their discrete form, using Scripps Clinic and Research Foundation (SCRF) normal ranges as cutpoints. RBC count, WBC count, hemoglobin, hematocrit, and platelet count were trichotomized as abnormal low, normal, and abnormal high. However, due to the sparse number of participants with abnormally high hematocrit values, the abnormal high category was combined with the normal category, resulting in contrasts of "normal or abnormal high" versus "abnormal low." Likewise, due to the sparse number of participants with abnormally low platelet counts, the discrete analysis of platelet counts contrasts "abnormal low or normal" versus "abnormal high."

The RBC morphology dependent variable was constructed from a number of laboratory conditions, many of which were minor abnormalities. These conditions were rouleaux, slight rouleaux, few Burr cells, few macrocytes, few ovalocytes, few target cells, moderate macrocytes, moderate stomatocytes, moderate anisocytosis, slight anisocytosis, slight polychromasia, slight baso-strippling, moderate microcytes, few Howell-Jolly bodies, and few schistocytes.

The SCRF laboratory coefficients of variation for the cell counts and indices meet or exceed requirements due to the precision of the Coulter S Plus® automated instrument, in conjunction with fast initial response cumulative sum (FIR CUSUM) quality control techniques. The SCRF laboratory normal values varied to some extent from the Kelsey-Seybold Clinic norms used at the Baseline examination. The SCRF laboratory normal values for all variables subsequently are shown.

Participants testing positive for the human immunosuppressant virus (HIV) (3 Ranch Hands and 1 Comparison) were excluded from the analysis of all variables. Participants with a fever (body temperature greater than or equal to 100° Fahrenheit) at the time of the examination were excluded from the analysis of all variables except prothrombin time. Participants taking an anticoagulant (Coumadin®) or aspirin at the time of the examination also were excluded from the analysis of prothrombin time.

Covariates

Age, race, military occupation, current level of cigarette smoking (cigarettes/day), and lifetime cigarette smoking history (pack-years) were used as candidate covariates in adjusted statistical analyses evaluating the hematologic dependent variables. Current cigarette smoking and lifetime cigarette smoking history were based on self-reported questionnaire

data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime, assuming 365 packs of cigarettes equal 1 pack-year. The smoking covariates were used in their continuous form for logistic regression and general linear models analyses and were discretized as necessary for tabular presentations of interactions between these covariates and exposure.

Statistical Methods

Table 16-1 summarizes the statistical analyses performed for the hematologic assessment. The first part of this table describes the dependent variables analyzed. The second part of this table provides a further description of the candidate covariates examined. Abbreviations used in the body of the table are defined at the end of the table. Chapter 7, Statistical Methods, describes the basic statistical analysis methods used in the Hematologic Assessment. Table 16-2 provides the number of participants with missing dependent variable and covariate data and those excluded due to medical conditions.

The variables absolute neutrophils (bands), absolute eosinophils, and absolute basophils had a substantial number of measurements equal to 0 counts per mm^3. The nonzero measurements exhibited a positively skewed distribution, and a logarithmic transformation enhanced the assumption of a normal distribution for these measurements. However, the logarithmic transformation cannot be applied to the measurements equal to 0 counts per mm^3. Consequently these variables were analyzed in two forms: (1) a discrete analysis of the proportion of zero measurements and (2) a continuous analysis of the nonzero measurements.

Analyses of data collected at the 1987 followup study indicated that dioxin was associated with military occupation. In general, enlisted personnel had higher levels of dioxin than officers, with enlisted groundcrew having higher levels than enlisted flyers. Consequently, adjustment for military occupation in statistical models using dioxin as a measure of exposure may improperly mask an actual dioxin effect. However, occupation also can be a surrogate for socioeconomic effects. Failure to adjust for occupation could overlook important risk factors related to lifestyle. If occupation was found to be significantly associated with a dependent variable in the 1992 followup analyses and was retained in the final statistical models using dioxin as a measure of exposure, the dioxin effect was evaluated in the context of two models. Analyses were performed with and without occupation in the final models to investigate whether conclusions regarding the association between the health endpoint and dioxin differed.

The results of the analyses without occupation are presented in Appendix L-3 and are only discussed in the text if the level of significance differs from the original final adjusted model (significant versus nonsignificant).

Longitudinal Analysis

Longitudinal analyses on platelet count were conducted to evaluate the association of exposure to changes between the 1982 Baseline examination and the 1992 followup examination.

Table 16-1.
Statistical Analyses for the Hematologic Assessment
Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Red Blood Cell (RBC) Count (million/mm^3)	LAB	D/C	Abnormal Low: <4.3 Normal: 4.3-5.9 Abnormal High: >5.9	AGE,RACE, OCC,CSMOK, PACKYR	U:PR,CS, GLM,TT A:PR,GLM
White Blood Cell (WBC) Count (thousand/mm^3)	LAB	D/C	Abnormal Low: <4.5 Normal: 4.5-11.0 Abnormal High: >11.0	AGE,RACE, OCC,CSMOK, PACKYR	U:PR,CS, GLM,TT A:PR,GLM
Hemoglobin (gm/dl)	LAB	D/C	Abnormal Low: <13.9 Normal: 13.9-18.0 Abnormal High: >18.0	AGE,RACE, OCC,CSMOK, PACKYR	U:PR,CS, GLM,TT A:PR,GLM
Hematocrit (percent)	LAB	D/C	Abnormal Low: <39.0 Normal or Abnormal High: ≥39.0	AGE,RACE, OCC,CSMOK, PACKYR	U:LR,CS, GLM,TT A:LR,GLM
Platelet Count (thousand/mm^3)	LAB	D/C	Abnormal High: >400.0 Abnormal Low or Normal: ≤400.0	AGE,RACE, OCC,CSMOK, PACKYR	U:LR,CS, GLM,TT A:LR,GLM L:LR,GLM
Prothrombin Time (seconds)	LAB	D/C	High: >13.2 Normal: ≤13.2	AGE,RACE, OCC,CSMOK, PACKYR	U:LR,CS, GLM,TT A:LR,GLM
RBC Morphology	LAB	D	Abnormal Normal	AGE,RACE, OCC,CSMOK, PACKYR	U:LR,CS A:LR
Absolute Neutrophils (segs) (thousand/mm^3)	LAB	C	--	AGE,RACE, OCC,CSMOK, PACKYR	U:GLM,TT A:GLM
Absolute Neutrophils (bands) (thousand/mm^3)	LAB	D/C	Zero Nonzero	AGE,RACE, OCC,CSMOK, PACKYR	U:LR,CS, GLM,TT A:GLM
Absolute Lymphocytes (thousand/mm^3)	LAB	C	--	AGE,RACE, OCC,CSMOK, PACKYR	U:GLM,TT A:GLM
Absolute Monocytes (thousand/mm^3)	LAB	C	--	AGE,RACE, OCC,CSMOK, PACKYR	U:GLM,TT A:GLM
Absolute Eosinophils (thousand/mm^3)	LAB	D/C	Zero Nonzero	AGE,RACE, OCC,CSMOK, PACKYR	U:LR,CS, GLM,TT A:GLM
Absolute Basophils (thousand/mm^3)	LAB	D/C	Zero Nonzero	AGE,RACE, OCC,CSMOK, PACKYR	U:LR,CS, GLM,TT A:GLM

Table 16-1. (Continued)
Statistical Analyses for the Hematologic Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born ≥1942 Born <1942
Race (RACE)	MIL	D	Black Non-Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Current Cigarette Smoking (CSMOK) (cigarettes/day)	Q-SR	D/C	0-Never 0-Former >0-20 >20
Lifetime Cigarette Smoking History (PACKYR) (pack-years)	Q-SR	D/C	0 >0-10 >10

Abbreviations

Data Source:
- LAB = 1992 laboratory results
- MIL = Air Force military records
- Q-SR = Health questionnaires (self-reported)

Data Form:
- C = Continuous analysis only
- D = Discrete analysis only
- D/C = Discrete and continuous analyses for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates

Statistical Analyses:
- U = Unadjusted analyses
- A = Adjusted analyses
- L = Longitudinal analyses

Statistical Methods:
- CS = Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
- GLM = General linear models analysis
- LR = Logistic regression analysis
- PR = Polychotomous logistic regression analysis
- TT = Two-sample t-test

Table 16-2.
Number of Participants with Missing Data for, or Excluded from, the Hematologic Assessment

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Red Blood Cell (RBC) Count	DEP	0	1	0	0	0	0
White Blood Cell (WBC) Count	DEP	0	1	0	0	0	0
Hemoglobin	DEP	0	1	0	0	0	0
Hematocrit	DEP	0	1	0	0	0	0
Platelet Count	DEP	0	2	0	0	0	1
Prothrombin Time	DEP	0	1	0	0	0	0
RBC Morphology	DEP	0	1	0	0	0	0
Absolute Neutrophils (segs)	DEP	0	1	0	0	0	0
Absolute Neutrophils (bands)	DEP	0	1	0	0	0	0
Absolute Lymphocytes	DEP	0	1	0	0	0	0
Absolute Monocytes	DEP	0	1	0	0	0	0
Absolute Eosinophils	DEP	0	1	0	0	0	0
Absolute Basophils	DEP	0	1	0	0	0	0
Current Cigarette Smoking	COV	0	2	0	0	0	2
Lifetime Cigarette Smoking History	COV	1	2	0	1	1	2
HIV Positive	EXC	3	1	2	3	3	1

Table 16-2. (Continued)
Number of Participants with Missing Data for, or Excluded from, the Hematologic Assessment

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Body Temperature Greater than or Equal to 100° Fahrenheit	EXC	3	1	1	3	3	1
Participants Taking an Anticoagulant or Aspirin	EXC	80	103	44	75	75	83

Abbreviations: DEP = Dependent variable (missing data).
COV = Covariate (missing data).
EXC = Exclusion.

Note: 952 Ranch Hands and 1,281 Comparisons;
520 Ranch Hands for initial dioxin; 894 Ranch Hands for current dioxin;
894 Ranch Hands and 1,063 Comparisons for categorized dioxin.
One Ranch Hand missing total lipids for current dioxin.

RESULTS

Dependent Variable-Covariate Associations

Results of the tests of association between the hematology dependent variables and covariates are presented in Appendix Table L-1-1. These associations are based on combined group data. Participants who tested positive for HIV were excluded from the analyses of all variables; participants with a fever at the time of the examination were excluded from the analyses of all variables except prothrombin time; participants who were taking an anticoagulant or aspirin at the time of the examination also were excluded from the analysis of prothrombin time.

Examining the association between the covariates and RBC count, in continuous form, revealed significant associations with age ($p<0.001$), race ($p=0.021$), occupation ($p<0.001$), and current cigarette smoking ($p<0.001$). RBC count decreased with age ($r=-0.143$). Blacks had a higher mean RBC count (5.11 million/mm^3) than non-Blacks (5.01 million/mm^3). Mean RBC count was highest for enlisted groundcrew (5.07 million/mm^3), followed by enlisted flyers (5.02 million/mm^3) and officers (4.96 million/mm^3). RBC count was positively associated with current cigarette smoking; that is, RBC count tended to increase as the number of cigarettes per day increased ($r=0.083$).

RBC count, in discrete form, was significantly associated with age ($p=0.047$), race ($p<0.001$), and occupation ($p=0.029$). The percentage of older participants with abnormally low RBC counts (3.5%) was greater than the percentage of younger participants with abnormally low RBC counts (1.8%). The percentages of older and younger participants with abnormally high RBC counts were equal (1.3%). The percentage of Blacks with abnormally high RBC counts (5.3%) was significantly greater than the percentage of non-Blacks with abnormally high RBC counts (1.1%). Percentages of Blacks and non-Blacks with abnormally low RBC counts were similar (3.1% for Blacks and 2.8% for non-Blacks). The percentage of participants with abnormally high RBC counts was greater for enlisted flyers and enlisted groundcrew (1.7% for both categories) than for officers (0.7%); the percentage of participants with abnormally low RBC counts was greater for officers (3.9%) than for enlisted personnel (1.9% for enlisted flyers and 2.1% for enlisted groundcrew).

Highly significant associations were found between WBC count, in continuous form, and race ($p<0.001$), occupation ($p<0.001$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p<0.001$). In contrast to RBC count, non-Blacks had a higher mean WBC count (7.43 thousand/mm^3) than Blacks (6.58 thousand/mm^3). Enlisted personnel had higher mean WBC counts (7.62 thousand/mm^3 for enlisted groundcrew, 7.77 thousand/mm^3 for enlisted flyers) than officers (6.95 thousand/mm^3). WBC count increased as current cigarette smoking increased ($r=0.438$) and lifetime cigarette smoking history increased ($r=0.245$).

WBC count in discrete form also was significantly associated with race ($p<0.001$), occupation ($p=0.002$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p<0.001$). The percentage of participants with abnormally low WBC counts was greater for Blacks (13.0%) than for non-Blacks (3.1%), while the percentage with

abnormally high WBC counts was greater for non-Blacks (5.7%) than Blacks (3.1%). The percentage of participants with abnormally low WBC counts was 4.1, 4.1, and 3.2 percent for officers, enlisted flyers, and enlisted groundcrew. The percentage of participants with abnormally high WBC counts was 3.4, 8.8, and 6.3 percent for officers, enlisted flyers, and enlisted groundcrew. The percentage of participants with abnormally low WBC counts decreased as the levels of current and lifetime cigarette smoking increased, while the percentage with abnormally high WBC counts increased as the levels of smoking increased.

Hemoglobin, in continuous form, was significantly associated with age ($p<0.001$), race ($p<0.001$), occupation ($p=0.007$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p=0.007$). The association between hemoglobin and age was negative ($r=-0.089$). The hemoglobin mean was greater for non-Blacks (15.89 gm/dl) than for Blacks (15.41 gm/dl) and increased from officers (15.78 gm/dl) to enlisted flyers (15.90 gm/dl) and enlisted groundcrew (15.93 gm/dl). Hemoglobin was positively associated with current cigarette smoking ($r=0.227$) and lifetime cigarette smoking history ($r=0.057$).

In discrete form, hemoglobin was significantly associated only with race ($p=0.001$) and current cigarette smoking ($p<0.001$). A greater percentage of Blacks had abnormally low hemoglobin levels (7.6%) than non-Blacks (2.3%), while a smaller percentage of Blacks had abnormally high levels (0.8%) than non-Blacks (1.9%). The percentage of participants with abnormally low hemoglobin levels decreased as current cigarette smoking increased, while the percentage of participants with abnormally high levels increased as current smoking increased.

Similar to hemoglobin, hematocrit in continuous form was significantly associated with all of the candidate covariates ($p<0.003$ for all covariates) and was significantly associated only with race ($p=0.048$) and current cigarette smoking ($p=0.032$) in discrete form. The association with hematocrit in continuous form was negative for age ($r=-0.067$) and was positive for current cigarette smoking ($r=0.239$) and lifetime cigarette smoking history ($r=0.072$). The hematocrit mean was greater for non-Blacks (46.33 percent) than for Blacks (45.48 percent) and increased from officers (45.98 percent) to enlisted flyers (46.42 percent) and enlisted groundcrew (46.49 percent). The percentage of Blacks with abnormally low hematocrit levels (3.8%) was greater than the percentage of non-Blacks (1.3%) and the percentage of non-smokers with abnormally low hematocrit levels (1.6% for participants who never smoked and 2.0% for former smokers) was greater than the percentage of smokers (0.3% for >0-20 cigarettes/day and 0.0% for >20 cigarettes/day).

Platelet count, in continuous form, was negatively associated with age ($p<0.001$, $r=-0.114$) and positively associated with current cigarette smoking ($p<0.001$, $r=0.109$) and lifetime cigarette smoking history ($p<0.001$, $r=0.091$). Platelet count also was significantly associated with occupation ($p<0.001$), where the platelet count means increased from officers (243.9 thousand/mm^3) to enlisted flyers (251.9 thousand/mm^3) and enlisted groundcrew (257.6 thousand/mm^3).

Platelet count, in discrete form, was associated only with occupation ($p=0.040$) and current cigarette smoking ($p=0.011$). Within each occupation category, the percentage of participants with abnormally high platelet counts were 0.5 percent for officers, 1.1 percent

for enlisted flyers, and 1.7 percent for enlisted groundcrew. The percentage of participants with abnormally high platelet counts increased with the levels of current cigarette smoking (0.8% for current non-smokers, 1.4% for >0-20 cigarettes/day, and 3.3% for >20 cigarettes/day).

Race, current cigarette smoking, and lifetime cigarette smoking history were significantly associated with prothrombin time in continuous form ($p=0.018$, $p<0.001$, and $p=0.007$ respectively). Blacks had a greater mean prothrombin time (12.09 seconds) than non-Blacks (11.93 seconds). The associations of prothrombin time with current cigarette smoking and lifetime cigarette smoking history were negative ($r=-0.140$ and $r=-0.060$). Discretized prothrombin time was significantly associated with age only, where 1.1 percent of the older participants had abnormally high prothrombin times while only 0.2 percent of the younger participants had abnormally high prothrombin times ($p=0.033$).

RBC morphology was significantly associated with age ($p<0.001$), race ($p=0.012$), and occupation ($p=0.046$). The percentage of older participants with abnormal RBC morphology measurements (50.5%) was greater than the percentage of younger participants (38.8%). A greater percentage of Blacks (56.5%) had abnormal RBC morphology measurements than did non-Blacks (44.8%). The percentage of participants with abnormal RBC morphology measurements within each occupation category was 47.3 percent for officers, 49.0 percent for enlisted flyers, and 42.7 percent for enlisted groundcrew.

Significant associations with absolute neutrophils (segs) were found for race, occupation, current cigarette smoking, and lifetime cigarette smoking history ($p<0.001$ for all associations). Mean absolute neutrophil (segs) counts were greater for non-Blacks (4.28 thousand/mm^3) than for Blacks (3.54 thousand/mm^3). Absolute neutrophil (segs) means were 3.96 thousand/mm^3 for officers, 4.45 thousand/mm^3 for enlisted flyers, and 4.40 thousand/mm^3 for enlisted groundcrew. The associations of absolute neutrophils (segs) with current cigarette smoking and lifetime cigarette smoking history were positive ($r=0.426$ and $r=0.242$ respectively).

Absolute neutrophils (bands), restricted to non-zero values, were significantly associated with race ($p=0.003$), current cigarette smoking ($p<0.001$, $r=0.229$), and lifetime cigarette smoking history ($p<0.001$, $r=0.129$). The mean absolute neutrophil (bands) count was greater for non-Blacks (0.261 thousand/mm^3) than for Blacks (0.185 thousand/mm^3). When contrasting zero versus non-zero absolute neutrophil (bands) measurements, a significant association was found with race ($p<0.001$). The percentage of Blacks with 0 absolute neutrophils (bands) per mm^3 was 32.8 percent in contrast to 15.7 percent of non-Blacks.

Absolute lymphocytes was significantly associated with occupation ($p<0.001$), current cigarette smoking ($p<0.001$, $r=0.164$), and lifetime cigarette smoking history ($p<0.001$, $r=0.087$). Mean absolute lymphocyte counts were 1.94 thousand/mm^3 for officers, 2.24 thousand/mm^3 for enlisted flyers, and 2.16 thousand/mm^3 for enlisted groundcrew.

For absolute monocytes, significant positive associations were found with current cigarette smoking ($p<0.001$, $r=0.184$) and lifetime cigarette smoking history ($p<0.001$, $r=0.109$).

Restricted to nonzero counts, absolute eosinophils was significantly associated with race ($p=0.021$), current cigarette smoking ($p<0.001$, $r=0.147$), and lifetime cigarette smoking history ($p<0.001$, $r=0.080$). The mean absolute eosinophil count was greater for non-Blacks (0.220 thousand/mm^3) than for Blacks (0.189 thousand/mm^3). Discretized absolute eosinophil values (zero versus nonzero) were not significantly associated with any of the candidate covariates.

For absolute basophils, restricted to nonzero values, significant positive associations were found with current cigarette smoking ($p<0.001$, $r=0.199$) and lifetime cigarette smoking history ($p<0.001$, $r=0.105$).

Exposure Analysis

The following section presents the results of the statistical analyses of the dependent variables shown in Table 16-1. Dependent variables are based on data derived from the laboratory portion of the 1992 followup examination.

Unadjusted and adjusted analyses of six models are presented for each variable. Model 1 examines the relationship between the dependent variable and group (Ranch Hand or Comparison). Model 2 explores the relationship between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin level greater than 10 ppt. If a participant did not have a 1987 dioxin level, a 1992 level was used. A statistical adjustment for the percent of body fat at the participant's time of duty in SEA and the change in the percent body fat from the time of duty in SEA to the date of the blood draw for dioxin is included in this model to account for body-fat-related differences in elimination rate (30). Model 3 dichotomizes the Ranch Hands in Model 2 based on their initial dioxin measures; these two categories of Ranch Hands are referred to as the "low Ranch Hand" category and the "high Ranch Hand" category. These participants are added to Ranch Hands and Comparisons with current serum dioxin levels (1987, if available; 1992, if the 1987 level was not available) at or below 10 ppt to create a total of four categories. Ranch Hands with current serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. The relationship between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the "Comparison" category is examined. A fourth contrast, exploring the relationship of the dependent variable in the low Ranch Hand category and the high Ranch Hand category combined, also is conducted. This combination is referred to in the text and tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment is made for percent body fat at the participant's time of duty in SEA and the change in the percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Models 4, 5, and 6 examine the relationship between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, a 1992 measurement was utilized in determining the current dioxin level. The measure of dioxin in Model 4 is lipid-adjusted, whereas whole-weight dioxin is used in Models 5 and 6. Model 6 differs from Model 5 in that a statistical adjustment for total lipids is included in Model 6. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7 respectively.

Results of investigations for group-by-covariate and dioxin-by-covariate interactions are referenced in the text, and tabular results are presented in Appendix L-2. As described previously, additional analyses were performed when occupation was retained in the final model for Models 2 through 6. Results excluding occupation from these models are tabled in Appendix L-3, and dioxin-by-covariate interactions with occupation excluded from these models are presented in Appendix L-4. Results from analyses excluding occupation are discussed in the text only if a meaningful change in the results occurred (that is, changes between significant results, marginally significant results, and nonsignificant results.

Laboratory Examination Variables

Red Blood Cell (RBC) Count (Continuous)

The unadjusted Model 1 analysis of RBC count in its continuous form revealed nonsignificant results (Table 16-3(a): $p>0.10$ for all contrasts). A highly significant interaction between group and current cigarette smoking was disclosed in the adjusted analysis (Table 16-3(b): $p=0.006$). Appendix Table L-2-1 shows stratified results from further analysis on the interaction. The results of the analysis displayed in Appendix Table L-2-1 showed a marginally significantly higher mean for Comparison former smokers than for Ranch Hand former smokers ($p=0.070$, Ranch Hand: 5.000 million/mm^3 and Comparison 5.044 million/mm^3). For heavy current smokers (>20 cigarettes/day), the Ranch Hand mean was marginally significantly higher than the Comparison mean ($p=0.076$, Ranch Hand: 5.163 million/mm^3 and Comparison: 5.070 million/mm^3). Additional covariates retained in the adjusted analysis included age, race, occupation, and lifetime cigarette smoking history.

Results from both the unadjusted and adjusted Model 2 analyses of RBC count were nonsignificant (Table 16-3(c,d): $p>0.12$ for both analyses). Race, lifetime cigarette smoking history, and the age-by-current cigarette smoking interaction were retained in the adjusted analysis. In the unadjusted Model 3 analysis, significant differences between Comparisons and the four Ranch Hand categories were not evident (Table 16-3(e): $p>0.17$ for all contrasts). The adjusted analysis showed a significant interaction between categorized dioxin and current cigarette smoking (Table 16-3(f): $p=0.027$). Stratified results from the investigation of the categorized dioxin-by-current smoking interaction are found in Appendix Table L-2-1. Analysis with this interaction removed revealed marginally significant differences between Comparisons and high Ranch Hands and low plus high Ranch Hands, with Comparisons having a higher mean RBC count than Ranch Hands ($p=0.095$, Diff. of Adj. Means=-0.045 for high Ranch Hands vs. Comparisons, and $p=0.065$, Diff. of Adj. Means=-0.038 for low plus high Ranch Hands vs. Comparisons). Covariates retained in the adjusted analysis were age, race, occupation, and lifetime cigarette smoking history. Without occupation in the final model, all contrasts became nonsignificant (Appendix Table L-3-1: $p>0.15$ for all contrasts).

Current dioxin displayed a marginally significant relationship with RBC count in the unadjusted Model 4 analysis (Table 16-3(g): $p=0.072$, Slope=0.0162). However, after adjusting for race, lifetime cigarette smoking history, and the age-by-current cigarette smoking interaction, the association was no longer significant (Table 16-3(h): $p=0.190$).

Table 16-3.
Analysis of Red Blood Cell (RBC) Count (million/mm^3)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***946***	***5.009***	***-0.019 (-0.052,0.013)***	***0.243***
	Comparison	***1,278***	***5.028***		
Officer	Ranch Hand	364	4.956	-0.007 (-0.059,0.044)	0.779
	Comparison	501	4.964		
Enlisted Flyer	Ranch Hand	162	4.986	-0.064 (-0.140,0.013)	0.105
	Comparison	201	5.050		
Enlisted Groundcrew	Ranch Hand	420	5.063	-0.014 (-0.062,0.035)	0.585
	Comparison	576	5.076		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks[a]
All	***Ranch Hand***	***945***	****	****	****	GROUP*CSMOK (p=0.006)
	Comparison	***1,276***	****			AGE (p<0.001)
Officer	Ranch Hand	363	****	****	****	RACE (p=0.071)
	Comparison	501	****			OCC (p=0.004)
Enlisted Flyer	Ranch Hand	162	****	****	****	PACKYR (p=0.038)
	Comparison	201	****			
Enlisted Groundcrew	Ranch Hand	420	****	****	****	
	Comparison	574	****			

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

**** Group-by-covariate interaction ($p \leq 0.01$); adjusted mean, difference of adjusted means, confidence interval, and p-value not presented; refer to Appendix Table L-2-1 for further analysis this interaction.

Table 16-3. (Continued)
Analysis of Red Blood Cell (RBC) Count (million/mm^3)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	174	4.974	4.980	0.021	0.0201 (0.0130)	0.122
Medium	172	5.015	5.017			
High	171	5.042	5.035			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[b]			
Initial Dioxin	n	Adj. Mean[b]	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Low	174	5.046	0.055	0.0127 (0.0135)	0.347	RACE (p=0.073)
Medium	172	5.067				PACKYR (p=0.089)
High	171	5.071				AGE*CSMOK (p=0.021)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-3. (Continued)
Analysis of Red Blood Cell (RBC) Count (million/mm^3)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,061	5.025	5.025		
Background RH	371	4.988	5.000	-0.025 (-0.070,0.021)	0.289
Low RH	259	4.990	4.989	-0.036 (-0.088,0.016)	0.175
High RH	258	5.031	5.018	-0.007 (-0.059,0.045)	0.801
Low plus High RH	517	5.010	5.003	-0.021 (-0.062,0.019)	0.299

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[b]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value	Covariate Remarks
Comparison	1,059	5.060**			DXCAT*CSMOK (p=0.027) AGE (p=0.001) RACE (p=0.041) OCC (p=0.019) PACKYR (p=0.015)
Background RH	370	5.057**	-0.003 (-0.049,0.043)**	0.897**	
Low RH	259	5.030**	-0.030 (-0.082,0.021)**	0.246**	
High RH	258	5.015**	-0.045 (-0.098,0.008)**	0.095**	
Low plus High RH	517	5.023**	-0.038 (-0.078,0.002)**	0.065**	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-1 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
DXCAT = Categorized Dioxin.

Table 16-3. (Continued)
Analysis of Red Blood Cell (RBC) Count (million/mm^3)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Mean/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)	p-Value
4	4.986 (292)	4.973 (299)	5.044 (297)	0.004	0.0162 (0.0089)	0.072
5	4.979 (297)	4.980 (297)	5.045 (294)	0.005	0.0157 (0.0077)	0.042
6[b]	4.988 (296)	4.980 (297)	5.035 (294)	0.008	0.0109 (0.0083)	0.188

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Current Dioxin Category Adjusted Mean/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	5.040 (291)	5.040 (299)	5.080 (297)	0.058	0.0118 (0.0090)	0.190	RACE (p=0.033) PACKYR (p=0.004) AGE*CSMOK (p=0.005)
5	5.033 (296)	5.044 (297)	5.083 (294)	0.059	0.0130 (0.0077)	0.089	RACE (p=0.032) PACKYR (p=0.004) AGE*CSMOK (p=0.005)
6[c]	5.050 (295)	5.050 (297)	5.072 (294)	0.064	0.0063 (0.0083)	0.445	RACE (p=0.022) PACKYR (p=0.003) AGE*CSMOK (p=0.004)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Adjusted for log_2 total lipids.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The Model 5 unadjusted analysis of RBC count disclosed a significant relationship with current whole-weight dioxin (Table 16-3(g): $p=0.042$, Slope=0.0157). The relationship became marginally significant after adjusting for covariate information (Table 16-3(h): $p=0.089$, Slope=0.0130). Results from both the unadjusted and adjusted Model 6 analyses were not significant ($p>0.18$ for both analyses). Race, lifetime cigarette smoking history, and the age-by-current cigarette smoking interaction were retained in the Model 5 and 6 adjusted analyses.

Red Blood Cell (RBC) Count (Discrete)

Both unadjusted and adjusted Model 1 analyses of RBC count revealed marginally significant differences overall between Ranch Hands and Comparisons for the abnormal low RBC count versus normal contrasts (Table 16-4(a,b): $p=0.087$, Est. RR=1.56 and $p=0.092$, Adj. RR=1.55 respectively). All other Model 1 contrasts were nonsignificant (Table 16-4(a,b): $p\geq0.16$ for all remaining contrasts). Age and race were significant covariates in the final adjusted model.

All Model 2 results examining the association between discrete RBC counts and initial dioxin were nonsignificant in the unadjusted and adjusted analyses (Table 16-4(c,d): $p>0.33$ for each contrast). Race was included in the final adjusted model.

Model 3 analysis of RBC count revealed a significant difference between background Ranch Hands and Comparisons from the unadjusted abnormal low versus normal RBC count contrast (Table 16-4(e): $p=0.049$, Est. RR=1.91). The difference was marginally significant for the analogous contrast in the adjusted analysis (Table 16-4(f): $p=0.084$, Adj. RR=1.77). The unadjusted low Ranch Hands versus Comparisons contrast was marginally significant for the examination of abnormal low versus normal RBC counts (Table 16-4(e): $p=0.063$, Est. RR=1.95). All other contrasts in Model 3 were nonsignificant (Table 16-4(e,f): $p>0.10$ for each remaining contrast). The age-by-race interaction was significant in the final adjusted model.

All results from Models 4, 5, and 6 analyzing the association between discrete RBC counts and current dioxin were nonsignificant for both the unadjusted and adjusted analyses (Table 16-4(g,h): $p>0.26$ for each contrast). Each model adjusted for the covariate effects of race, current cigarette smoking, and lifetime cigarette smoking history.

White Blood Cell (WBC) Count (Continuous)

While the unadjusted Model 1 analysis of WBC count yielded only nonsignificant results (Table 16-5(a): $p>0.28$), the adjusted analysis led to a significant group-by-race interaction (Table 16-5(b): $p=0.023$). Appendix Table L-2-2 presents results for Ranch Hands versus Comparisons stratified by race. Differences between Ranch Hands and Comparisons in mean WBC count, computed after removing the interaction, were not significant ($p>0.55$ for all contrasts). Age, lifetime cigarette smoking history, and the current cigarette smoking-by-occupation interaction were included in the final model.

Table 16-4.
Analysis of Red Blood Cell (RBC) Count
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal Low	Percent Normal	Percent Abnormal High	Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***Ranch Hand***	***946***	***3.5***	***95.2***	***1.3***	***1.56 (0.94,2.58)***	***0.087***	***0.97 (0.46,2.03)***	***0.926***
	Comparison	***1,278***	***2.3***	***96.4***	***1.3***				
Officer	Ranch Hand	364	4.7	94.8	0.6	1.39 (0.70,2.76)	0.345	0.70 (0.13,3.82)	0.676
	Comparison	501	3.4	95.8	0.8				
Enlisted Flyer	Ranch Hand	162	2.5	96.9	0.6	1.64 (0.36,7.43)	0.522	0.25 (0.03,2.11)	0.201
	Comparison	201	1.5	96.0	2.5				
Enlisted Groundcrew	Ranch Hand	420	2.9	95.0	2.1	1.87 (0.78,4.48)	0.161	1.58 (0.61,4.13)	0.354
	Comparison	576	1.6	97.1	1.4				

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value	Covariate Remarks[a]
All	***1.55 (0.93,2.57)***	***0.092***	***0.96 (0.46,2.03)***	***0.919***	AGE ($p<0.001$) RACE ($p=0.004$)
Officer	1.37 (0.69,2.74)	0.366	0.68 (0.12,3.72)	0.654	
Enlisted Flyer	1.62 (0.36,7.39)	0.530	0.25 (0.03, 2.21)	0.213	
Enlisted Groundcrew	1.87 (0.78,4.51)	0.160	1.59 (0.61,4.18)	0.346	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-4. (Continued)
Analysis of Red Blood Cell (RBC) Count
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Percent			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	174	4.6	94.8	0.6	0.80 (0.52,1.22)	0.305	1.03 (0.59,1.79)	0.918
Medium	172	2.9	94.2	2.9				
High	171	1.8	97.7	0.6				

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)[c]					
	Abnormal Low vs. Normal		Abnormal Low vs. Normal		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
517	0.81 (0.53,1.24)	0.333	1.06 (0.60,1.90)	0.833	RACE (p=0.122)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-4. (Continued)
Analysis of Red Blood Cell (RBC) Count
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

		Percent			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	2.4	96.3	1.3				
Background RH	371	4.3	94.9	0.8	1.91 (1.00,3.65)	0.049	0.77 (0.22,2.73)	0.686
Low RH	259	4.6	93.8	1.5	1.95 (0.96,3.95)	0.063	1.06 (0.33,3.38)	0.919
High RH	258	1.6	97.3	1.2	0.64 (0.22,1.86)	0.410	0.66 (0.18,2.39)	0.525
Low plus High RH	517	3.1	95.6	1.4	1.29 (0.68,2.45)	0.436	0.84 (0.33,2.17)	0.722

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

		Abnormal Low vs. Normal		Abnormal High vs. Normal		
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,061					AGE*RACE (p=0.040)
Background RH	371	1.77 (0.93,3.39)	0.084	0.79 (0.22,2.84)	0.723	
Low RH	259	1.80 (0.88,3.66)	0.107	0.98 (0.31,3.15)	0.974	
High RH	258	0.75 (0.26,2.20)	0.603	0.75 (0.20,2.77)	0.668	
Low plus High RH	517	1.33 (0.70,2.54)	0.383	0.87 (0.34,2.24)	0.769	

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of duty in SEA and change in body fat from the time of duty in SEA to the date of the blood draw for dioxin.
[c] Adjusted for percent body fat at the time of duty in SEA, change in body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-4. (Continued)
Analysis of Red Blood Cell (RBC) Count
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED									
	Current Dioxin Category Summary Statistics					Analysis Results for Log_2 (Current Dioxin + 1)			
			Percent			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Model[a]	Current Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
4	Low	292	4.1	94.9	1.0	0.87 (0.67,1.12)	0.285	1.18 (0.79,1.77)	0.423
	Medium	299	4.4	95.3	0.3				
	High	297	2.4	95.6	2.0				
5	Low	297	4.0	95.0	1.0	0.89 (0.72,1.09)	0.268	1.16 (0.81,1.67)	0.417
	Medium	297	4.4	95.0	0.7				
	High	294	2.4	95.9	1.7				
6[c]	Low	296	4.1	94.9	1.0	0.90 (0.73,1.12)	0.359	1.20 (0.82,1.75)	0.356
	Medium	297	4.4	95.0	0.7				
	High	294	2.4	95.9	1.7				

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 16-4. (Continued)
Analysis of Red Blood Cell (RBC) Count
(Discrete)

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED						
		Analysis Results for Log_2 (Current Dioxin + 1)				
		Abnormal Low vs. Normal		Abnormal High vs. Normal		
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	887	0.88 (0.68,1.15)	0.349	1.21 (0.79,1.86)	0.377	RACE (p=0.026) CSMOK (p=0.092) PACKYR (p=0.027)
5	887	0.90 (0.73,1.11)	0.331	1.20 (0.82,1.76)	0.354	RACE (p=0.025) CSMOK (p=0.090) PACKYR (p=0.027)
6[c]	886	0.92 (0.73,1.15)	0.447	1.23 (0.82,1.84)	0.308	RACE (p=0.031) CSMOK (p=0.095) PACKYR (p=0.024)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 16-5.
Analysis of White Blood Cell (WBC) Count (thousand/mm^3)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***946***	***7.15***	***0.09 --***	***0.305***
	Comparison	***1,278***	***7.06***		
Officer	Ranch Hand	364	6.75	0.04 --	0.704
	Comparison	501	6.70		
Enlisted Flyer	Ranch Hand	162	7.37	0.02 --	0.924
	Comparison	201	7.35		
Enlisted Groundcrew	Ranch Hand	420	7.43	0.14 --	0.282
	Comparison	576	7.29		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***945***	***6.66*****	***0.03 --*****	0.690**	GROUP*RACE (p=0.023)
	Comparison	***1,276***	***6.63*****			AGE (p<0.001)
Officer	Ranch Hand	363	6.37**	0.03 --**	0.771**	PACKYR (p=0.002)
	Comparison	501	6.34**			CSMOK*OCC (p=0.025)
Enlisted Flyer	Ranch Hand	162	6.66**	-0.08 --**	0.656**	
	Comparison	201	6.73**			
Enlisted Groundcrew	Ranch Hand	420	6.93**	0.06 --**	0.551**	
	Comparison	574	6.87**			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-2 for further analysis of this interaction.

Table 16-5. (Continued)
Analysis of White Blood Cell (WBC) Count (thousand/mm^3)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	6.87	6.88	0.012	0.0161 (0.0097)	0.100
Medium	172	7.40	7.42			
High	171	7.34	7.31			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	6.50**	0.283**	0.0019 (0.0098)**	0.846**	INIT*RACE (p=0.008) INIT*OCC (p=0.028) CSMOK (p<0.001) PACKYR (p=0.018)
Medium	172	6.68**				
High	171	6.60**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of WBC count versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table L-2-2 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
INIT = Log_2 (initial dioxin).

Table 16-5. (Continued)
Analysis of White Blood Cell (WBC) Count (thousand/mm^3)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.L.)[c]	p-Value[d]
Comparison	1,061	7.05	7.05		
Background RH	371	7.00	7.03	-0.02 --	0.838
Low RH	259	7.06	7.05	0.00 --	0.999
High RH	258	7.34	7.31	0.26 --	0.058
Low plus High RH	517	7.20	7.18	0.13 --	0.221

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,059	6.62			PACKYR ($p<0.001$) AGE*RACE ($p=0.007$) CSMOK*OCC ($p=0.016$)
Background RH	370	6.64	0.03 --	0.792	
Low RH	259	6.66	0.04 --	0.726	
High RH	258	6.64	0.02 --	0.828	
Low plus High RH	517	6.65	0.03 --	0.713	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin $>$ 10 ppt, 10 ppt $<$ Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin $>$ 10 ppt, Initial Dioxin $>$ 143 ppt.

Table 16-5. (Continued)
Analysis of White Blood Cell (WBC) Count (thousand/mm^3)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	6.99 (292)	7.02 (299)	7.34 (297)	0.002	0.0093 (0.0066)	0.162
5	6.95 (297)	7.02 (297)	7.39 (294)	0.003	0.0086 (0.0057)	0.130
6[d]	7.02 (296)	7.02 (297)	7.30 (294)	0.013	0.0035 (0.0061)	0.571

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	6.53** (291)	6.53** (299)	6.57** (297)	0.263	0.0013 (0.0067)**	0.850**	CURR*RACE (p=0.041) PACKYR (p=0.011) AGE*RACE (p=0.032) CSMOK*OCC (p=0.022)
5	6.50** (296)	6.52** (297)	6.62** (294)	0.264	0.0014 (0.0056)**	0.803**	CURR*RACE (p=0.019) PACKYR (p=0.011) AGE*RACE (p=0.030) CSMOK*OCC (p=0.022)
6[e]	6.53** (295)	6.54** (297)	6.59** (294)	0.265	-0.0009 (0.0061)**	0.879**	CURR*RACE (p=0.019) PACKYR (p=0.014) AGE*RACE (p=0.025) CSMOK*OCC (p=0.031)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of WBC count versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-2 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.
CURR = Log_2 (current dioxin + 1).

A marginally significant dose-response relationship between initial dioxin and WBC count was disclosed in the unadjusted Model 2 analysis (Table 16-5(c): $p=0.100$, Slope=0.0161). Adjusting for covariates caused the association to become nonsignificant (Table 16-5(d): $p=0.846$). Two significant initial dioxin interactions involving race and occupation were retained in the adjusted analysis ($p=0.008$ and $p=0.028$ respectively) as were the covariates of current cigarette smoking and lifetime cigarette smoking history. Appendix Table L-2-2 contains information on the association between WBC count and initial dioxin stratified by race and occupation. Results cited for the final adjusted model reflect removal of the initial dioxin-by-race and initial dioxin-by-occupation interactions.

The Model 3 unadjusted analysis revealed that Ranch Hands in the high category possess a marginally significantly greater mean WBC count level than do Comparisons (Table 16-5(e): $p=0.058$, Diff. of Adj. Mean=0.26). Other contrasts between Ranch Hands and Comparisons examined in the unadjusted analysis were nonsignificant ($p>0.22$). Furthermore, no significant results were found after adjusting for lifetime cigarette smoking history and the age-by-race and current cigarette smoking-by-occupation interactions (Table 16-5(f): $p>0.71$ for all contrasts).

Unadjusted and adjusted results examining the relationship between WBC count and current dioxin were nonsignificant for each of Models 4, 5, and 6 (Table 16-5(g,h): $p\geq0.13$ for all analyses). Each adjusted analysis retained the current dioxin-by-race interaction as well as lifetime cigarette smoking history and the age-by-race and current cigarette smoking-by-occupation interactions. Final adjusted model results are based on the exclusion of the current dioxin-by-race interaction. Results stratified by race that examine the association between current dioxin and WBC count are found in Appendix Table L-2-2. When occupation was removed from the final model, the association between current dioxin and WBC count became marginally significant in Models 4 and 5 (Appendix Table L-3-2: $p=0.061$, Slope=0.0111 for Model 4; $p=0.058$, Slope=0.0096 for Model 5).

White Blood Cell (WBC) Count (Discrete)

Each unadjusted and adjusted analysis of discrete WBC counts was nonsignificant for all contrasts and associations examined in Models 1, 2, and 3 (Table 16-6(a-f): $p>0.12$ for each contrast). Each model adjusted for age, race, occupation, and current cigarette smoking in the final adjusted model. However, after excluding occupation from the Model 2 adjusted analysis, the association with initial dioxin was marginally significant for the abnormal high versus normal contrast (Table L-3-3: $p=0.096$, Adj. RR=0.74), showing a decrease in the percentage of abnormally high WBC counts as initial dioxin increased.

Adjusted analyses of discrete WBC counts in Models 4 and 6 revealed a significant inverse relationship between abnormally high WBC counts and current dioxin (Table 16-6(h): $p=0.029$, Adj. RR=0.79 and $p=0.034$, Adj. RR=0.83 respectively). Results were marginally significant for the Model 5 adjusted analysis (Table 16-6(h): $p=0.081$, Adj. RR=0.87). All other unadjusted and adjusted analyses were nonsignificant (Table 16-6(g,h): $p>0.22$ for all remaining contrasts). Each model adjusted for the significant covariate effects of occupation and lifetime cigarette smoking history as well as the current dioxin-by-race and age-by-race interactions. Each adjusted analysis is based on the final model after

Table 16-6.
Analysis of White Blood Cell (WBC) Count
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal Low	Percent Normal	Percent Abnormal High	Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***Ranch Hand***	***946***	***3.8***	***90.0***	***6.2***	***1.07 (0.69,1.67)***	***0.756***	***1.24 (0.87,1.79)***	***0.237***
	Comparison	***1,278***	***3.6***	***91.3***	***5.1***				
Officer	Ranch Hand	364	3.9	92.3	3.9	0.92 (0.46,1.84)	0.819	1.29 (0.62,2.71)	0.498
	Comparison	501	4.2	92.8	3.0				
Enlisted Flyer	Ranch Hand	162	5.6	85.2	9.3	1.93 (0.67,5.56)	0.221	1.14 (0.55,2.36)	0.728
	Comparison	201	3.0	88.6	8.5				
Enlisted Groundcrew	Ranch Hand	420	3.1	89.8	7.1	0.95 (0.46,1.95)	0.891	1.26 (0.76,2.11)	0.370
	Comparison	576	3.3	91.0	5.7				

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value	Covariate Remarks[a]
All	***1.11 (0.70,1.75)***	***0.654***	***1.18 (0.80,1.74)***	***0.400***	AGE (p=0.002) RACE (p<0.001) OCC (p=0.005) CSMOK (p<0.001)
Officer	0.92 (0.46,1.85)	0.815	1.33 (0.60,2.95)	0.480	
Enlisted Flyer	1.95 (0.66,5.77)	0.226	0.97 (0.44,2.10)	0.931	
Enlisted Groundcrew	1.05 (0.50,2.20)	0.903	1.24 (0.72,2.13)	0.443	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-6. (Continued)
Analysis of White Blood Cell (WBC) Count
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Percent			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	174	6.3	87.4	6.3	0.94 (0.67,1.33)	0.740	0.90 (0.67,1.20)	0.457
Medium	172	2.9	90.1	7.0				
High	171	3.5	91.8	4.7				

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)[c]					
Abnormal Low vs. Normal			Abnormal High vs. Normal		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
517	0.94 (0.60,1.46)	0.778	0.75 (0.52,1.08)	0.127	AGE (p=0.007) RACE (p=0.018) OCC (p=0.130) CSMOK (p<0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-6. (Continued)
Analysis of White Blood Cell (WBC) Count
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

		Percent			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	3.3	91.4	5.3				
Background RH	371	3.5	90.6	5.9	0.95 (0.49,1.83)	0.884	1.07 (0.64,1.78)	0.808
Low RH	259	4.6	88.4	7.0	1.51 (0.77,2.97)	0.232	1.41 (0.81,2.45)	0.223
High RH	258	3.9	91.1	5.0	1.31 (0.64,2.70)	0.462	1.01 (0.54,1.87)	0.987
Low plus High RH	517	4.3	89.8	6.0	1.41 (0.82,2.45)	0.217	1.21 (0.77,1.90)	0.418

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

		Abnormal Low vs. Normal		Abnormal High vs. Normal		
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,059					AGE (p=0.011) RACE (p<0.001) OCC (p=0.099) CSMOK (p<0.001)
Background RH	371	1.06 (0.54,2.11)	0.861	1.11 (0.63,1.96)	0.709	
Low RH	259	1.26 (0.62,2.58)	0.521	1.53 (0.86,2.75)	0.151	
High RH	258	1.37 (0.63,3.00)	0.431	0.79 (0.41,1.52)	0.477	
Low plus High RH	517	1.31 (0.73,2.34)	0.369	1.11 (0.69,1.80)	0.664	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-6. (Continued)
Analysis of White Blood Cell (WBC) Count
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED									
	Current Dioxin Category Summary Statistics					Analysis Results for Log_2 (Current Dioxin + 1)			
			Percent			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Model[a]	Current Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
4	Low	292	3.8	90.4	5.8	1.00 (0.79,1.26)	0.984	0.88 (0.73,1.08)	0.224
	Medium	299	4.4	89.0	6.7				
	High	297	3.7	90.9	5.4				
5	Low	297	3.7	90.9	5.4	1.00 (0.82,1.22)	0.982	0.93 (0.79,1.09)	0.380
	Medium	297	4.7	88.2	7.1				
	High	294	3.4	91.2	5.4				
6[c]	Low	296	3.7	90.9	5.4	1.02 (0.82,1.25)	0.873	0.91 (0.76,1.07)	0.259
	Medium	297	4.7	88.2	7.1				
	High	294	3.4	91.2	5.4				

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 16-6. (Continued)
Analysis of White Blood Cell (WBC) Count
(Discrete)

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED						
		Analysis Results for Log_2 (Current Dioxin + 1)				
		Abnormal Low vs. Normal		Abnormal High vs. Normal		
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	887	1.04 (0.77,1.39)**	0.821**	0.79 (0.65,0.98)**	0.029**	CURR*RACE (p=0.044) OCC (p=0.019) PACKYR (p<0.001) AGE*RACE (p=0.009)
5	887	1.06 (0.82,1.37)**	0.660**	0.87 (0.74,1.02)**	0.081**	CURR*RACE (p=0.036) OCC (p=0.023) PACKYR (p<0.001) AGE*RACE (p=0.007)
6[c]	886	1.04 (0.80,1.36)**	0.769**	0.83 (0.70,0.99)**	0.034**	CURR*RACE (p=0.026) OCC (p=0.027) PACKYR (p<0.001) AGE*RACE (p=0.006)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-3 for further analysis of this interaction.

deletion of the current dioxin-by-race interaction. Results stratified by race for each model are presented in Appendix Table L-2-3. After excluding occupation from each final adjusted model for Models 4, 5, and 6, all contrasts were nonsignificant (Appendix Table L-3-3: $p > 0.10$ for each contrast).

Hemoglobin (Continuous)

None of the contrasts examining differences in mean hemoglobin for Ranch Hands versus Comparisons were significant in the Model 1 analyses (Table 16-7(a,b): $p > 0.38$ for all contrasts). Two significant group interactions involving current cigarette smoking and lifetime cigarette smoking history were disclosed in the adjusted analysis (Table 16-7(b): $p = 0.008$ and $p = 0.036$ respectively). Appendix Table L-2-4 shows results from separate analyses on these interactions, stratified by the levels of each covariate. Results were nonsignificant after removal of the group-by-covariate interactions from the model ($p > 0.50$ for all contrasts). Other significant covariates in the adjusted analysis included age, race, and the lifetime cigarette smoking history-by-occupation interaction.

Mean levels of hemoglobin increased significantly with initial dioxin in the unadjusted Model 2 analysis (Table 16-7(c): $p = 0.029$, Slope$=0.0792$). However, adjustment for race and the age-by-current cigarette smoking interaction caused this finding to become nonsignificant (Table 16-7(d): $p = 0.179$).

All associations with hemoglobin from the Model 3 categorized dioxin unadjusted and adjusted analyses were nonsignificant (Table 16-7(e,f): $p > 0.12$) although, analogous to Model 1, two group interactions involving current cigarette smoking and lifetime cigarette smoking history were retained in the adjusted analysis ($p = 0.007$ and $p = 0.019$). Stratified results from additional analyses of these terms are shown in Appendix Table L-2-4. Final adjusted results were calculated with the interactions excluded from the final model. Age, race, and the current cigarette smoking-by-occupation interaction also were retained in the adjusted analysis.

No significant associations between current dioxin and hemoglobin were disclosed in the unadjusted and adjusted analyses for Model 4, 5, and 6 (Table 16-7(g,h): $p > 0.23$ for all analyses). Race, lifetime cigarette smoking history, and the age-by-current cigarette smoking interaction were significant in each of the adjusted analyses.

Hemoglobin (Discrete)

Except for the adjusted abnormal high versus normal contrast among officers in Model 1, all unadjusted and adjusted analyses of hemoglobin in discrete form revealed nonsignificant results (Table 16-8(a-h): $p > 0.11$ for each contrast). Within the officer stratum, the Model 1 adjusted analysis revealed a marginally significant difference in the percentage of Ranch Hands with abnormally high hemoglobin levels versus Comparisons (Table 16-8(b): $p = 0.095$, Adj. RR$=2.33$). Models 1 and 3 adjusted for the covariate effects of current cigarette smoking and the age-by-race interaction. Model 2 adjusted for current cigarette smoking only, and Models 4, 5, and 6 each adjusted for the race-by-current cigarette smoking interaction.

Table 16-7.
Analysis of Hemoglobin (gm/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***946***	***15.87***	***0.01 (-0.08,0.10)***	***0.818***
	Comparison	***1,278***	***15.86***		
Officer	Ranch Hand	364	15.81	0.04 (-0.09,0.18)	0.527
	Comparison	501	15.76		
Enlisted Flyer	Ranch Hand	162	15.87	-0.07 (-0.29,0.16)	0.553
	Comparison	201	15.93		
Enlisted Groundcrew	Ranch Hand	420	15.93	0.01 (-0.12,0.14)	0.912
	Comparison	576	15.92		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks[a]
All	***Ranch Hand***	***945***	***15.62*****	***-0.00 (-0.09,0.08)*****	0.944**	GROUP*CSMOK (p=0.008) GROUP*PACKYR (p=0.036) AGE (p=0.014) RACE (p<0.001) PACKYR*OCC (p=0.004)
	Comparison	***1,276***	***15.63*****			
Officer	Ranch Hand	363	15.61**	0.05 (-0.09,0.18)**	0.509**	
	Comparison	501	15.57**			
Enlisted Flyer	Ranch Hand	162	15.60**	-0.09 (-0.30,0.11)**	0.384**	
	Comparison	201	15.69**			
Enlisted Groundcrew	Ranch Hand	420	15.63**	-0.01 (-0.14,0.11)**	0.849**	
	Comparison	574	15.64**			

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interactions ($p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table L-2-4 for further analysis of these interactions.

Table 16-7. (Continued)
Analysis of Hemoglobin (gm/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	174	15.74	15.74	0.009	0.0792 (0.0361)	0.029
Medium	172	15.83	15.83			
High	171	16.00	16.01			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[b]			
Initial Dioxin	n	Adj. Mean[b]	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Low	174	15.64	0.071	0.0496 (0.0369)	0.179	RACE (p=0.037) AGE*CSMOK (p=0.026)
Medium	172	15.63				
High	171	15.81				

[a] Adjusted for percent body fat at the time of duty in the SEA and change in percent body fat from the time of duty in the SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in the SEA, change in percent body fat from the time of duty in the SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-7. (Continued)
Analysis of Hemoglobin (gm/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,061	15.86	15.86		
Background RH	371	15.86	15.87	0.01 (-0.11,0.13)	0.876
Low RH	259	15.75	15.75	-0.11 (-0.24,0.03)	0.128
High RH	258	15.97	15.96	0.10 (-0.04,0.24)	0.159
Low plus High RH	517	15.85	15.85	0.00 (-0.11,0.10)	0.941

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[b]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value	Covariate Remarks
Comparison	1,059	15.65**			DXCAT*CSMOK (p=0.007)
					DXCAT*PACKYR (p=0.019)
Background RH	370	15.68**	0.03 (-0.09,0.15)**	0.615**	AGE (p=0.060)
Low RH	259	15.57**	-0.08 (-0.21,0.06)**	0.259**	RACE (p<0.001)
High RH	258	15.66**	0.01 (-0.13,0.15)**	0.863**	PACKYR*OCC (p=0.002)
Low plus High RH	517	15.62**	-0.03 (-0.14,0.07)**	0.544**	

[a] Adjusted for percent body fat at the time of duty in the SEA and change in percent body fat from the time of duty in the SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in the SEA, change in percent body fat from the time of duty in the SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interactions ($p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table L-2-4 for further analysis of these interactions.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-7. (Continued)
Analysis of Hemoglobin (gm/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Mean/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)	p-Value
4	15.88 (292)	15.75 (299)	15.95 (297)	0.001	0.0237 (0.0244)	0.332
5	15.85 (297)	15.77 (297)	15.95 (294)	0.002	0.0250 (0.0209)	0.232
6[b]	15.85 (296)	15.77 (297)	15.95 (294)	0.008	0.0088 (0.0225)	0.696

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Current Dioxin Category Adjusted Mean/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	15.71 (291)	15.63 (299)	15.75 (297)	0.095	0.0166 (0.0239)	0.487	RACE (p=0.010) PACKYR (p=0.004) AGE*CSMOK (p=0.032)
5	15.69 (296)	15.95 (297)	15.75 (294)	0.095	0.0202 (0.0204)	0.322	RACE (p=0.010) PACKYR (p=0.004) AGE*CSMOK (p=0.030)
6[c]	15.75 (295)	15.66 (297)	15.72 (294)	0.099	0.0048 (0.0221)	0.826	RACE (p=0.015) PACKYR (p=0.003) AGE*CSMOK (p=0.028)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Adjusted for log_2 total lipids.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 16-8.
Analysis of Hemoglobin
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal Low	Percent Normal	Percent Abnormal High	Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***Ranch Hand***	***946***	***3.0***	***94.7***	***2.3***	***1.24 (0.74,2.08)***	***0.419***	***1.59 (0.85,2.95)***	***0.144***
	Comparison	***1,278***	***2.4***	***96.1***	***1.5***				
Officer	Ranch Hand	364	2.5	94.5	3.0	0.69 (0.31,1.56)	0.374	2.17 (0.83,5.67)	0.112
	Comparison	501	3.6	95.0	1.4				
Enlisted Flyer	Ranch Hand	162	3.7	94.4	1.9	2.57 (0.63,10.47)	0.186	3.86 (0.40,37.64)	0.245
	Comparison	201	1.5	98.0	0.5				
Enlisted Groundcrew	Ranch Hand	420	3.1	95.0	1.9	1.81 (0.79,4.16)	0.164	1.01 (0.40,2.54)	0.980
	Comparison	576	1.7	96.4	1.9				

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value	Covariate Remarks[a]
All	***1.26 (0.75,2.13)***	***0.386***	***1.56 (0.83,2.93)***	***0.170***	CSMOK (p<0.001)
Officer	0.68 (0.30,1.54)	0.355	2.33 (0.86,6.31)	0.095	AGE*RACE (p=0.001)
Enlisted Flyer	2.59 (0.63,10.65)	0.187	3.44 (0.34,35.03)	0.297	
Enlisted Groundcrew	1.95 (0.83,4.55)	0.123	0.97 (0.39,2.46)	0.955	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-8. (Continued)
Analysis of Hemoglobin
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Percent			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	174	2.9	94.8	2.3	0.91 (0.59,1.40)	0.669	1.09 (0.71,1.67)	0.689
Medium	172	2.9	95.9	1.2				
High	171	1.8	95.3	2.9				

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)[c]					
	Abnormal Low vs. Normal		Abnormal High vs. Normal		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
517	0.93 (0.61,1.42)	0.732	1.07 (0.68,1.68)	0.765	CSMOK (p=0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-8. (Continued)
Analysis of Hemoglobin
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

		Percent			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	2.3	96.2	1.5				
Background RH	371	3.5	94.6	1.9	1.63 (0.81,3.25)	0.170	1.44 (0.58,3.55)	0.434
Low RH	259	3.9	94.2	1.9	1.65 (0.78,3.51)	0.192	1.25 (0.45,3.46)	0.667
High RH	258	1.2	96.5	2.3	0.49 (0.15,1.67)	0.256	1.37 (0.53,3.58)	0.516
Low plus High RH	517	2.5	95.4	2.1	1.08 (0.54,2.14)	0.835	1.31 (0.60,2.87)	0.493

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

		Abnormal Low vs. Normal		Abnormal High vs. Normal		
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,059					CSMOK ($p<0.001$) AGE*RACE ($p=0.006$)
Background RH	371	1.59 (0.79,3.19)	0.197	1.26 (0.48,3.28)	0.635	
Low RH	259	1.38 (0.64,2.98)	0.414	1.24 (0.43,3.53)	0.691	
High RH	258	0.58 (0.17,1.98)	0.382	1.49 (0.56,3.98)	0.423	
Low plus High RH	517	1.05 (0.52,2.12)	0.897	1.37 (0.61,3.04)	0.446	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-8. (Continued)
Analysis of Hemoglobin
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED									
	Current Dioxin Category Summary Statistics					Analysis Results for Log_2 (Current Dioxin + 1)			
			Percent			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Model[a]	Current Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
4	Low	292	3.8	94.2	2.1	0.92 (0.70,1.21)	0.542	1.13 (0.83,1.54)	0.448
	Medium	299	3.3	94.7	2.0				
	High	297	1.7	96.3	2.0				
5	Low	297	3.4	95.0	1.7	0.92 (0.73,1.16)	0.477	1.14 (0.86,1.50)	0.359
	Medium	297	3.7	94.3	2.0				
	High	294	1.7	95.9	2.4				
6[c]	Low	296	3.4	94.9	1.7	0.94 (0.74,1.20)	0.634	1.15 (0.86,1.53)	0.340
	Medium	297	3.7	94.3	2.0				
	High	294	1.7	95.9	2.4				

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 16-8. (Continued)
Analysis of Hemoglobin
(Discrete)

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED						
		Analysis Results for Log_2 (Current Dioxin + 1)				
		Abnormal Low vs. Normal		Abnormal High vs. Normal		
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	888	0.91 (0.68,1.23)	0.548	1.20 (0.88,1.65)	0.242	RACE*CSMOK (p=0.002)
5	888	0.91 (0.70,1.18)	0.486	1.19 (0.90,1.56)	0.219	RACE*CSMOK (p=0.002)
6[c]	887	0.93 (0.71,1.22)	0.610	1.23 (0.92,1.64)	0.165	RACE*CSMOK (p=0.002)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Hematocrit (Continuous)

For Ranch Hands versus Comparisons, no significant differences in mean hematocrit levels were disclosed in the Model 1 unadjusted analysis (Table 16-9(a): $p>0.42$ for all contrasts). In the adjusted analysis, two group interactions were retained, one involving current cigarette smoking and the other involving lifetime cigarette smoking history (Table 16-9(b): $p=0.006$ and $p=0.015$). When these terms were deleted from the final model, differences between the two groups were nonsignificant ($p>0.42$ for all contrasts). Race and the lifetime cigarette smoking history-by-occupation interaction were additionally significant in the adjusted analysis. Appendix Table L-2-5 presents stratified results for the two group interaction terms.

The Model 2 unadjusted analysis revealed a significant positive association between hemoglobin and initial dioxin (Table 16-9(c): $p=0.015$, Slope=0.2647). The association was marginally significant after adjusting for the age-by-current cigarette smoking interaction (Table 16-9(d): $p=0.057$, Slope=0.2117). In the unadjusted Model 3 analysis, Ranch Hands in the low category possessed a marginally significant lower mean level of hematocrit (45.89 percent) than Comparisons (46.25 percent), (Table 16-9(e): $p=0.100$, Diff. of Adj. Means= -0.36). Results were nonsignificant in the adjusted analysis (Table 16-9(f): $p>0.13$ for all contrasts). The categorized dioxin-by-current cigarette smoking and the categorized dioxin-by-lifetime cigarette smoking history interactions were significant in the adjusted analysis ($p=0.002$ and $p=0.008$). Final adjusted results reflect analyses omitting these interactions. Further investigation of the interactions was performed and results are found in Appendix Table L-2-5.

Current dioxin and hematocrit were not significantly associated in the Model 4, 5, and 6 unadjusted and adjusted analyses (Table 16-9(g,h): $p>0.18$ for all analyses). Each of the final models were adjusted for lifetime cigarette smoking history and the age-by-current cigarette smoking interaction.

Hematocrit (Discrete)

The unadjusted and adjusted Model 1 analyses of hematocrit, in discrete form, displayed no significant differences between Ranch Hands and Comparisons (Table 16-10(a,b): $p>0.15$). Covariates retained in the adjusted model were age, race, current cigarette smoking, and lifetime cigarette smoking history.

Analyses of Model 2 found no significant association between hematocrit and initial dioxin (Table 16-10(c,d): $p>0.28$ for both analyses). Age and lifetime cigarette smoking history were retained in the final adjusted model. The unadjusted Model 3 analysis of hematocrit showed a marginally significant difference between background Ranch Hands and Comparisons (Table 16-10(e): $p=0.096$, Est. RR=2.31). However, after adjusting for the effect of covariates, the contrast became nonsignificant (Table 16-10(f): $p=0.106$). All other contrasts were nonsignificant in the unadjusted and adjusted analyses ($p>0.48$ for all remaining contrasts). Covariates retained in the adjusted model were age, race, current cigarette smoking, and lifetime cigarette smoking history.

Table 16-9.
Analysis of Hematocrit (percent)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***946***	***46.30***	***0.03 (-0.24,0.29)***	***0.839***
	Comparison	***1,278***	***46.27***		
Officer	Ranch Hand	364	46.08	0.18 (-0.26,0.61)	0.426
	Comparison	501	45.90		
Enlisted Flyer	Ranch Hand	162	46.32	-0.19 (-0.86,0.49)	0.585
	Comparison	201	46.51		
Enlisted Groundcrew	Ranch Hand	420	46.48	-0.03 (-0.42,0.36)	0.888
	Comparison	576	46.51		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks[a]
All	***Ranch Hand***	***945***	***45.82*****	***-0.02 (-0.28,0.24)*****	***0.879*****	GROUP*CSMOK (p=0.006) GROUP*PACKYR (p=0.015) RACE (p<0.001) PACKYR*OCC (p<0.001)
	Comparison	***1,276***	***45.84*****			
Officer	Ranch Hand	363	45.73**	0.16 (-0.26,0.57)**	0.451**	
	Comparison	501	45.57**			
Enlisted Flyer	Ranch Hand	162	45.75**	-0.26 (-0.89,0.38)**	0.423**	
	Comparison	201	46.01**			
Enlisted Groundcrew	Ranch Hand	420	45.90**	-0.09 (-0.47,0.30)**	0.658**	
	Comparison	574	45.99**			

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interactions ($p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table L-2-5 for further analysis of these interactions.

Table 16-9. (Continued)
Analysis of Hematocrit (percent)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	174	45.82	45.82	0.011	0.2647 (0.1085)	0.015
Medium	172	46.16	46.16			
High	171	46.70	46.71			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[b]			
Initial Dioxin	n	Adj. Mean[b]	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Low	174	45.96	0.062	0.2117 (0.1110)	0.057	AGE*CSMOK (p=0.038)
Medium	172	46.07				
High	171	46.65				

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-9. (Continued)
Analysis of Hematocrit (percent)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,061	46.25	46.25		
Background RH	371	46.26	46.29	0.04 (-0.33,0.41)	0.835
Low RH	259	45.90	45.89	-0.36 (-0.78,0.07)	0.100
High RH	258	46.55	46.52	0.27 (-0.15,0.70)	0.209
Low plus High RH	517	46.22	46.21	-0.04 (-0.37,0.29)	0.802

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[b]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value	Covariate Remarks
Comparison	1,059	45.88**			DXCAT*CSMOK (p=0.002) DXCAT*PACKYR (p=0.008) RACE (p=0.002) CSMOK*OCC (p=0.047) PACKYR*OCC (p<0.001)
Background RH	370	45.98**	0.10 (-0.27,0.47)**	0.591**	
Low RH	259	45.56**	-0.31 (-0.72,0.10)**	0.138**	
High RH	258	45.89**	0.02 (-0.41,0.44)**	0.935**	
Low plus High RH	517	45.73**	-0.15 (-0.47,0.18)**	0.370**	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interactions ($p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table L-2-5 for further analysis of these interactions.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-9. (Continued)
Analysis of Hematocrit (percent)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Mean/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)	p-Value
4	46.29 (292)	45.91 (299)	46.51 (297)	0.001	0.0827 (0.0747)	0.268
5	46.22 (297)	45.96 (297)	46.54 (294)	0.002	0.0827 (0.0640)	0.197
6[b]	46.22 (296)	45.96 (297)	46.54 (294)	0.006	0.0397 (0.0691)	0.565

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Current Dioxin Category Adjusted Mean/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	46.27 (291)	46.02 (299)	46.43 (297)	0.091	0.0783 (0.0731)	0.285	PACKYR (p=0.004) AGE*CSMOK (p=0.017)
5	46.22 (296)	46.05 (297)	46.45 (294)	0.091	0.0824 (0.0624)	0.187	PACKYR (p=0.004) AGE*CSMOK (p=0.016)
6[c]	46.30 (295)	46.06 (297)	46.35 (294)	0.094	0.0414 (0.0678)	0.542	PACKYR (p=0.003) AGE*CSMOK (p=0.014)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Adjusted for log_2 total lipids.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 16-10.
Analysis of Hematocrit
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal Low	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***946***	***1.7***	***1.36 (0.68,2.73)***	***0.496***
	Comparison	***1,278***	***1.3***		
Officer	Ranch Hand	364	1.7	0.75 (0.27,2.04)	0.746
	Comparison	501	2.2		
Enlisted Flyer	Ranch Hand	162	2.5	5.06 (0.56,45.75)	0.250
	Comparison	201	0.5		
Enlisted Groundcrew	Ranch Hand	420	1.4	2.07 (0.58,7.39)	0.409
	Comparison	576	0.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.42 (0.70,2.88)***	***0.330***	AGE ($p<0.001$) RACE ($p=0.012$) CSMOK ($p=0.002$) PACKYR ($p=0.072$)
Officer	0.77 (0.28,2.12)	0.615	
Enlisted Flyer	4.97 (0.55,45.30)	0.155	
Enlisted Groundcrew	2.28 (0.63,8.27)	0.208	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-10. (Continued)
Analysis of Hematocrit
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal Low**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	1.2	1.22 (0.74,2.01)	0.439
Medium	172	1.2		
High	171	1.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
517	1.33 (0.79,2.24)	0.287	AGE (p=0.089) PACKYR (p=0.014)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-10. (Continued)
Analysis of Hematocrit
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal Low	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	0.9		
Background RH	371	1.9	2.31 (0.86,6.19)	0.096
Low RH	259	1.5	1.51 (0.47,4.89)	0.489
High RH	258	1.2	1.11 (0.30,4.09)	0.880
Low plus High RH	517	1.4	1.31 (0.49,3.48)	0.592

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,059			AGE (p=0.005) RACE (p=0.081) CSMOK (p=0.012) PACKYR (p=0.123)
Background RH	370	2.27 (0.84,6.14)	0.106	
Low RH	259	1.40 (0.43,4.56)	0.580	
High RH	258	1.38 (0.36,5.32)	0.638	
Low plus High RH	517	1.39 (0.51,3.76)	0.516	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-10. (Continued)
Analysis of Hematocrit
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal Low/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.7 (292)	1.7 (299)	1.4 (297)	1.16 (0.82,1.64)	0.417
5	1.4 (297)	2.0 (297)	1.4 (294)	1.08 (0.80,1.48)	0.608
6[c]	1.4 (296)	2.0 (297)	1.4 (294)	1.22 (0.87,1.71)	0.247

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	888	1.16 (0.82,1.65)	0.404	CSMOK (p=0.014)
5	888	1.10 (0.79,1.51)	0.582	CSMOK (p=0.014)
6[d]	887	1.21 (0.86,1.70)	0.282	CSMOK (p=0.020)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

No significant association between hematocrit and current dioxin was found in the unadjusted and adjusted analyses of Models 4, 5, and 6 (Table 16-10(g,h): $p>0.24$ for all analyses). Current cigarette smoking was the only significant covariate in each of the adjusted models.

Platelet Count (Continuous)

Overall, Ranch Hands possessed a significantly greater mean platelet count than Comparisons in the Model 1 unadjusted analysis (Table 16-11(a): $p=0.030$, Diff. of Means=5.1). Mean platelet count for Ranch Hands was 251.3 thousand/mm^3 in contrast to 246.2 thousand/mm^3 for Comparisons. Stratifying this analysis by occupation disclosed significant differences between Ranch Hands and Comparisons in both the enlisted flyer and enlisted groundcrew categories ($p=0.016$, Diff. of Means=14.1 for enlisted flyers and $p=0.011$, Diff. of Means=9.2 for enlisted groundcrew). Mean platelet count in the enlisted flyer stratum was 256.6 thousand/mm^3 for Ranch Hands and 242.5 thousand/mm^3 for Comparisons. In the enlisted groundcrew category, mean platelet count for Ranch Hands and Comparisons was 259.8 thousand/mm^3 and 250.7 thousand/mm^3 respectively. In the adjusted analysis, the interaction of group and occupation was significant (Table 16-11(b): $p=0.010$). Comparable to the unadjusted analysis, the Ranch Hands and Comparisons differed significantly overall and within the enlisted flyer and enlisted groundcrew strata (Table 16-11(b): $p=0.036$, Diff. of Adj. Mean=4.8; $p=0.014$, Diff. of Adj. Mean=13.9; and $p=0.010$, Diff. of Adj. Means=8.9 respectively). In each case, Ranch Hands possessed a greater mean level of platelet count than Comparisons. Age, current cigarette smoking, and lifetime cigarette smoking were included in the final model.

In the unadjusted Model 2 analysis, mean platelet count levels increased significantly with initial dioxin (Table 16-11(c): $p=0.025$, Slope=0.1270). However, adjustment for age, current cigarette smoking, and the lifetime cigarette smoking history-by-race interaction yielded nonsignificant results (Table 16-11(d): $p=0.267$).

In the Model 3 unadjusted analysis, the differences for the high Ranch Hand and the low plus high Ranch Hand categories versus the Comparison group were highly significant (Table 16-11(e): $p<0.001$, Diff. of Means=15.1 and $p=0.004$, Diff. of Mean=8.3 respectively). Mean platelet counts for the high and low plus high Ranch Hand categories were 260.8 and 254.0 thousand/mm^3 in contrast to only 245.7 thousand/mm^3 for Comparisons. These differences remained highly significant in the adjusted analysis. The adjusted mean platelet count was 258.5 thousand/mm^3 for high Ranch Hands, 253.1 thousand/mm^3 for low plus high Ranch Hands, and 245.8 thousand/mm^3 for Comparisons (Table 16-11(f): $p<0.001$ for high Ranch Hands vs. Comparisons and $p=0.010$ for low plus high Ranch Hands vs. Comparisons). The adjusted analysis retained age, current cigarette smoking, and lifetime cigarette smoking history.

Significant positive relationships between platelet count and current dioxin were found to exist in the Model 4, 5, and 6 unadjusted analyses (Table 16-11(g): $p=0.033$ Slope=0.0845, for Model 4; $p=0.018$, Slope=0.0800 for Model 5; and $p=0.045$, Slope= 0.0734, for Model 6). However, after adjusting for lifetime cigarette smoking history and the age-by-occupation interaction, the associations became nonsignificant and, in the case of

Table 16-11.
Analysis of Platelet Count (thousand/mm^3)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***946***	***251.3***	***5.1 --***	***0.030***
	Comparison	***1,277***	***246.2***		
Officer	Ranch Hand	364	239.3	-3.3 --	0.343
	Comparison	500	242.6		
Enlisted Flyer	Ranch Hand	162	256.6	14.1 --	0.016
	Comparison	201	242.5		
Enlisted Groundcrew	Ranch Hand	420	259.8	9.2 --	0.011
	Comparison	576	250.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***945***	***251.0****	***4.8 --****	***0.036****	GROUP*OCC (p=0.010)
	Comparison	***1,275***	***246.1****			AGE (p<0.001)
Officer	Ranch Hand	363	242.6	-3.6 --	0.324	CSMOK (p=0.036)
	Comparison	500	246.2			PACKYR (p<0.001)
Enlisted Flyer	Ranch Hand	162	256.2	13.9 --	0.014	
	Comparison	201	242.2			
Enlisted Groundcrew	Ranch Hand	420	256.7	8.9 --	0.010	
	Comparison	574	247.8			

[a] Transformed from the square root scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

[c] P-values based on difference of means on square root scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction.

Table 16-11. (Continued)
Analysis of Platelet Count (thousand/mm^3)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	245.9	245.8	0.029	0.1270 (0.0566)	0.025
Medium	172	252.9	252.4			
High	171	258.8	259.4			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	257.4	0.086	0.0645 (0.0580)	0.267	AGE ($p<0.001$)
Medium	172	259.6				CSMOK ($p=0.135$)
High	171	265.1				PACKYR*RACE ($p=0.029$)

[a] Transformed from square root scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on square root of platelet count versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-11. (Continued)
Analysis of Platelet Count (thousand/mm^3)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,060	245.7	245.7		
Background RH	371	247.2	245.1	-0.6 --	0.855
Low RH	259	245.8	247.3	1.6 --	0.669
High RH	258	259.2	260.8	15.1 --	<0.001
Low plus High RH	517	252.4	254.0	8.3 --	0.004

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ac]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,058	245.8			AGE (p<0.001) CSMOK (p=0.105) PACKYR (p<0.001)
Background RH	370	246.0	0.2 --	0.949	
Low RH	259	247.8	2.1 --	0.575	
High RH	258	258.5	12.7 --	<0.001	
Low plus High RH	517	253.1	7.3 --	0.010	

[a] Transformed from square root scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on square root scale.

[d] P-value is based on difference of means on square root scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-11. (Continued)
Analysis of Platelet Count (thousand/mm^3)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	247.2 (292)	245.7 (299)	258.0 (297)	0.005	0.0845 (0.0395)	0.033
5	245.6 (297)	248.9 (297)	256.4 (294)	0.006	0.0800 (0.0339)	0.018
6[d]	246.3 (296)	248.9 (297)	255.4 (294)	0.009	0.0734 (0.0366)	0.045

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	250.3 (291)	246.8 (299)	250.8 (297)	0.056	-0.0093 (0.0452)	0.836	PACKYR ($p<0.001$) AGE*OCC ($p=0.042$)
5	248.6 (296)	249.9 (297)	249.3 (294)	0.056	0.0105 (0.0380)	0.782	PACKYR ($p<0.001$) AGE*OCC ($p=0.048$)
6[e]	249.7 (295)	250.1 (297)	247.5 (294)	0.058	-0.0050 (0.0415)	0.904	PACKYR ($p=0.001$) AGE*OCC ($p=0.046$)

[a] Transformed from square root scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on square root of platelet count versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Models 4 and 6, negative (Table 16-11(h): p=0.836 for Model 4, p=0.782 for Model 5, and p=0.904 for Model 6).

Platelet Count (Discrete)

All unadjusted and adjusted analyses of platelet count in discrete form were nonsignificant in Models 1 and 2 (Table 16-12(a-d): p>0.16 for each analysis). Covariates in the final adjusted model for Model 1 were age, occupation, and current cigarette smoking. Model 2 adjusted for age only.

The unadjusted and adjusted analyses of platelet count in Model 3 revealed a significant difference between the high Ranch Hand category and the Comparison group (Table 16-12(e,f): p=0.027, Est. RR=3.12 and p=0.029, Adj. RR=3.10). Both analyses indicated that Ranch Hands in the high dioxin category had a greater percentage of abnormally high platelet counts than Comparisons (2.7% versus 0.9%). All other contrasts in Model 3 were nonsignificant (p>0.14 for each remaining contrast). Current cigarette smoking was the only significant covariate in the adjusted model.

Unadjusted analyses of platelet count in Models 4, 5, and 6 each displayed a significant positive association with current dioxin (Table 16-12(g): p=0.014, Est. RR=1.63; p=0.017, Est. RR=1.55; and p=0.016, Est. RR=1.60 respectively). The adjusted results in Model 4 are identical to the unadjusted results due to the absence of any significant covariate in the final adjusted model. The association with current dioxin was marginally significant in Model 5 after adjustment for age (Table 16-12(h): p=0.062, Adj. RR=1.42) and was nonsignificant in Model 6 after adjustment for current cigarette smoking (p=0.377).

Prothrombin Time (Continuous)

All contrasts investigating differences between Ranch Hands and Comparisons in the Model 1 analyses of prothrombin time were nonsignificant (Table 16-13(a,b): p>0.15 for all contrasts). The final model was adjusted for current cigarette smoking and the lifetime cigarette smoking history-by-race interaction.

Prothrombin time did not increase significantly with initial dioxin in the unadjusted Model 2 analysis (Table 16-13(c): p=0.337). However, in the adjusted analysis, a highly significant dose-response relationship between prothrombin time and initial dioxin was disclosed (Table 16-13(d): p=0.019, Slope=0.0033). Adjusted means for the low, medium, and high initial dioxin categories were 11.93, 11.96, and 11.98 seconds. Race, current cigarette smoking, and the age-by-lifetime cigarette smoking history interaction were retained in the final adjusted model. No significant differences between Ranch Hands and Comparisons were found in the unadjusted and adjusted analyses of prothrombin time for Model 3 (Table 16-13(e,f): p>0.13). The categorized dioxin-by-age interaction, race, occupation, and current cigarette smoking were significant in the adjusted analysis. Adjusted results are based on analysis after the deletion of the categorized dioxin-by-age interaction. Appendix Table L-2-6 contains results from further analysis on the categorized dioxin-by-age interaction.

Table 16-12.
Analysis of Platelet Count
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***946***	***1.4***	***1.47 (0.67,3.23)***	***0.449***
	Comparison	***1,277***	***0.9***		
Officer	Ranch Hand	364	0.3	0.46 (0.05,4.41)	0.851
	Comparison	500	0.6		
Enlisted Flyer	Ranch Hand	162	1.2	1.24 (0.17,8.93)	0.999
	Comparison	201	1.0		
Enlisted Groundcrew	Ranch Hand	420	2.4	1.98 (0.75,5.25)	0.248
	Comparison	576	1.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.45 (0.65,3.20)***	***0.362***	AGE (p=0.142) OCC (p=0.019) CSMOK (p=0.014)
Officer	0.47 (0.05,4.58)	0.517	
Enlisted Flyer	1.17 (0.16,8.42)	0.875	
Enlisted Groundcrew	1.95 (0.76,4.99)	0.167	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-12. (Continued)
Analysis of Platelet Count
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal High**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	0.6	1.38 (0.88,2.16)	0.174
Medium	172	1.7		
High	171	2.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
517	1.17 (0.71,1.93)	0.550	AGE (p=0.037)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-12. (Continued)
Analysis of Platelet Count
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,060	0.9		
Background RH	371	0.3	0.33 (0.04,2.66)	0.300
Low RH	259	0.8	0.86 (0.19,4.04)	0.853
High RH	258	2.7	3.12 (1.14,8.55)	0.027
Low plus High RH	517	1.7	1.97 (0.77,5.03)	0.156

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,058			CSMOK (p=0.006)
Background RH	371	0.34 (0.04,2.70)	0.306	
Low RH	259	0.91 (0.19,4.29)	0.905	
High RH	258	3.10 (1.13,8.54)	0.029	
Low plus High RH	517	2.02 (0.78,5.21)	0.145	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-12. (Continued)
Analysis of Platelet Count
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal High/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (292)	0.3 (299)	2.7 (297)	1.63 (1.11,2.39)	0.014
5	0.3 (297)	0.7 (297)	2.4 (294)	1.55 (1.09,2.20)	0.017
6[c]	0.3 (296)	0.7 (297)	2.4 (294)	1.60 (1.09,2.34)	0.016

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	888	1.63 (1.11,2.39)	0.014	
5	888	1.42 (0.98,2.05)	0.062	AGE (p=0.073)
6[d]	887	0.76 (0.42,1.38)	0.377	CSMOK (p=0.077)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 16-13.
Analysis of Prothrombin Time (seconds)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***869***	***11.93***	***0.01 --***	***0.765***
	Comparison	***1,176***	***11.92***		
Officer	Ranch Hand	336	11.93	0.02 --	0.504
	Comparison	457	11.90		
Enlisted Flyer	Ranch Hand	145	11.97	0.06 --	0.479
	Comparison	182	11.91		
Enlisted Groundcrew	Ranch Hand	388	11.92	-0.03 --	0.358
	Comparison	537	11.95		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***868***	***12.05***	***0.01 --***	0.662	CSMOK ($p<0.001$) PACKYR*RACE ($p<0.001$)
	Comparison	***1,174***	***12.04***			
Officer	Ranch Hand	335	12.02	0.02 --	0.582	
	Comparison	457	12.00			
Enlisted Flyer	Ranch Hand	145	12.10	0.08 --	0.155	
	Comparison	182	12.02			
Enlisted Groundcrew	Ranch Hand	388	12.04	-0.02 --	0.481	
	Comparison	535	12.07			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-13. (Continued)
Analysis of Prothrombin Time (seconds)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	157	11.90	11.91	0.040	0.0013 (0.0014)	0.337
Medium	157	11.90	11.91			
High	160	11.90	11.89			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	157	11.93**	0.113	0.0033 (0.0014)**	0.019**	CSMOK (p=0.001)
Medium	157	11.96**				RACE (p=0.088)
High	160	11.98**				AGE*PACKYR (p=0.028)

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of prothromobin time versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-13. (Continued)
Analysis of Prothrombin Time (seconds)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	979	11.92	11.92		
Background RH	342	11.94	11.95	0.03 --	0.328
Low RH	234	11.88	11.88	-0.05 --	0.171
High RH	240	11.92	11.91	-0.01 --	0.662
Low plus High RH	474	11.90	11.89	-0.03 --	0.245

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	977	11.97**			DXCAT*AGE (p=0.004) RACE (p=0.015) OCC (p=0.101) CSMOK (p<0.001)
Background RH	341	12.01**	0.04 --**	0.157**	
Low RH	234	11.92**	-0.05 --**	0.131**	
High RH	240	11.95**	-0.02 --**	0.590**	
Low plus High RH	474	11.93**	-0.03 --**	0.188**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-6 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-13. (Continued)
Analysis of Prothrombin Time (seconds)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	11.93 (269)	11.92 (270)	11.90 (277)	<0.001	-0.0002 (0.0009)	0.819
5	11.94 (271)	11.91 (273)	11.89 (272)	0.001	-0.0007 (0.0008)	0.412
6[d]	11.92 (270)	11.91 (273)	11.92 (272)	0.011	0.0002 (0.0009)	0.814

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	11.92 (268)	11.91 (270)	11.91 (277)	0.041	0.0001 (0.0009)	0.910	CSMOK (p<0.001) AGE*PACKYR (p=0.009)
5	11.94 (270)	11.90 (273)	11.91 (272)	0.041	-0.0004 (0.0008)	0.633	CSMOK (p<0.001) AGE*PACKYR (p=0.010)
6[e]	11.92 (269)	11.90 (273)	11.93 (272)	0.048	0.0004 (0.0009)	0.626	CSMOK (p<0.001) AGE*PACKYR (p=0.014)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of prothrombin time versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Prothrombin time and current dioxin were not significantly associated in any of the Model 4, 5, and Model 6 unadjusted and adjusted analyses (Table 16-13(g,h): $p>0.41$). Each adjusted analysis retained current cigarette smoking and the age-by-lifetime cigarette smoking history interaction.

Prothrombin Time (Discrete)

Ranch Hands and Comparisons did not display significantly different percentages of abnormally high prothrombin time in either the unadjusted or adjusted Model 1 analyses (Table 16-14(a,b): $p>0.39$). Age was the only covariate retained in the adjusted analysis.

All results from the Model 2 and Model 3 analyses exploring associations between prothrombin time and dioxin were nonsignificant (Table 16-14(c-f): $p>0.10$ for all analyses). Age was retained in each adjusted analysis and the occupation-by-lifetime cigarette smoking history interaction also was retained in Model 3.

Prothrombin time was not significantly associated with current dioxin in the Model 4, 5, and 6 unadjusted and adjusted analyses (Table 16-14(g,h): $p>0.38$ for all analyses). The Model 4 adjusted analysis contained a significant interaction between current dioxin and lifetime cigarette smoking history (Table 16-14(h): $p=0.047$). Final adjusted results are based upon analyses without the interaction. Further analysis of the interaction was performed and results are shown in Appendix Table L-2-7. Covariates retained in the final models included current cigarette smoking and the age-by-lifetime cigarette smoking history interaction for Model 4, age and current cigarette smoking history for Model 5, and age, current cigarette smoking, and lifetime cigarette smoking history for Model 6.

RBC Morphology

Results from the Model 1 group analyses of RBC morphology were nonsignificant (Table 16-15(a,b): $p>0.14$ for all analyses). Significant covariates included age and the race-by-occupation interaction.

Neither the unadjusted nor adjusted Model 2 analyses of RBC morphology revealed a significant association with initial dioxin (Table 16-15(c,d): $p>0.68$). Age and the race-by-lifetime cigarette smoking history interaction were retained in the adjusted analysis. Unadjusted analysis results for Model 3 were nonsignificant (Table 16-15(e): $p\geq0.11$ for all contrasts). In the adjusted analysis, a significant negative association between background Ranch Hands and Comparisons was disclosed (Table 16-15(f): $p=0.049$, Adj. $RR=0.78$). All other contrasts between Ranch Hands and Comparisons were nonsignificant ($p>0.46$). The final model was adjusted for age and the race-by-occupation interaction.

Each of the unadjusted Model 4, 5, and 6 analyses of RBC morphology were not significant (Table 16-15(g): $p>0.41$ for all analyses). After adjusting for age and the race-by-occupation interaction, positive associations between current dioxin and RBC morphology for each final model were either significant or marginally significant (Table 16-15(h): $p=0.083$, Adj. $RR=1.10$ for Model 4; $p=0.090$, Adj. $RR=1.08$ for Model 5; and $p=0.045$, Adj. $RR=1.11$ for Model 6). However, after removing occupation from the final

Table 16-14.
Analysis of Prothrombin Time
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***869***	***0.9***	***1.55 (0.56,4.30)***	***0.555***
	Comparison	***1,176***	***0.6***		
Officer	Ranch Hand	336	1.2	1.36 (0.34,5.50)	0.937
	Comparison	457	0.9		
Enlisted Flyer	Ranch Hand	145	1.4	1.26 (0.18,9.05)	0.999
	Comparison	182	1.1		
Enlisted Groundcrew	Ranch Hand	388	0.5	2.78 (0.25,30.74)	0.777
	Comparison	537	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.56 (0.56,4.34)***	***0.393***	AGE ($p < 0.001$)
Officer	1.41 (0.35,5.73)	0.628	
Enlisted Flyer	1.18 (0.16,8.62)	0.868	
Enlisted Groundcrew	2.77 (0.25,30.72)	0.406	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-14. (Continued)
Analysis of Prothrombin Time
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent High**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	157	1.3	0.47 (0.16,1.38)	0.101
Medium	157	1.3		
High	160	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
474	0.58 (0.16,2.12)	0.346	AGE (p=0.004)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-14. (Continued)
Analysis of Prothrombin Time
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	979	0.4		
Background RH	342	0.9	2.80 (0.61,12.78)	0.184
Low RH	234	1.3	2.50 (0.54,11.49)	0.239
High RH	240	0.4	0.79 (0.09,7.21)	0.832
Low plus High RH	474	0.8	1.62 (0.40,6.65)	0.503

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	977			AGE (p=0.028) OCC*PACKYR (p=0.037)
Background RH	341	2.38 (0.49,11.52)	0.280	
Low RH	234	1.81 (0.36,9.14)	0.474	
High RH	240	1.29 (0.10,16.11)	0.846	
Low plus High RH	474	1.67 (0.36,7.69)	0.513	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-14. (Continued)
Analysis of Prothrombin Time
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent High/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.7 (269)	1.5 (270)	0.4 (277)	0.82 (0.48,1.41)	0.462
5	0.7 (271)	1.5 (273)	0.4 (272)	0.83 (0.55,1.25)	0.386
6[c]	0.7 (270)	1.5 (273)	0.4 (272)	0.92 (0.58,1.46)	0.712

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	815	0.88 (0.46,1.68)**	0.698**	CURR*PACKYR (p=0.047) CSMOK (p=0.111) AGE*PACKYR (p=0.036)
5	816	0.82 (0.48,1.42)	0.483	AGE (p=0.011) CSMOK (p=0.064)
6[d]	814	0.98 (0.54,1.78)	0.950	AGE (p=0.058) CSMOK (p=0.053) PACKYR (p=0.117)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence Interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-7 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 16-15.
Analysis of RBC Morphology

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***946***	***44.6***	***0.94 (0.79,1.11)***	***0.493***
	Comparison	***1,278***	***46.2***		
Officer	Ranch Hand	364	47.3	1.00 (0.76,1.31)	0.999
	Comparison	501	47.3		
Enlisted Flyer	Ranch Hand	162	50.6	1.12 (0.74,1.70)	0.663
	Comparison	201	47.8		
Enlisted Groundcrew	Ranch Hand	420	40.0	0.83 (0.64,1.07)	0.164
	Comparison	576	44.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.93 (0.79,1.11)***	***0.436***	AGE ($p<0.001$) RACE*OCC ($p=0.006$)
Officer	0.99 (0.75,1.30)	0.945	
Enlisted Flyer	1.13 (0.74,1.73)	0.558	
Enlisted Groundcrew	0.82 (0.64,1.07)	0.144	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-15. (Continued)
Analysis of RBC Morphology

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	45.4	0.97 (0.85,1.11)	0.681
Medium	172	47.1		
High	171	44.4		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
517	1.02 (0.89,1.17)	0.773	AGE (p=0.075) RACE*PACKYR (p=0.032)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-15. (Continued)
Analysis of RBC Morphology

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	46.7		
Background RH	371	41.5	0.82 (0.65,1.05)	0.110
Low RH	259	46.3	0.96 (0.73,1.27)	0.788
High RH	258	45.0	0.93 (0.71,1.23)	0.618
Low plus High RH	517	45.7	0.95 (0.77,1.17)	0.618

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,061			AGE ($p<0.001$) RACE*OCC ($p=0.007$)
Background RH	371	0.78 (0.61,1.00)	0.049	
Low RH	259	0.90 (0.68,1.19)	0.469	
High RH	258	1.05 (0.79,1.40)	0.749	
Low plus High RH	517	0.97 (0.78,1.20)	0.779	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-15. (Continued)
Analysis of RBC Morphology

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	44.5 (292)	42.5 (299)	44.8 (297)	1.02 (0.93,1.12)	0.619
5	44.1 (297)	42.1 (297)	45.6 (294)	1.02 (0.95,1.11)	0.578
6[c]	43.9 (296)	42.1 (297)	45.6 (294)	1.04 (0.95,1.13)	0.417

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	888	1.10 (0.99,1.22)	0.083	AGE (p=0.008) RACE*OCC (p=0.022)
5	888	1.08 (0.99,1.19)	0.090	AGE (p=0.009) RACE*OCC (p=0.021)
6[d]	887	1.11 (1.00,1.22)	0.045	AGE (p=0.008) RACE*OCC (p=0.021)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

adjusted model, all three models become nonsignificant (Appendix Table L-3-9: $p > 0.11$ for all models).

Absolute Neutrophils (segs)

Significant differences between Ranch Hands and Comparisons did not exist in the Model 1 unadjusted and adjusted analyses of absolute neutrophils (segs) (Table 16-16(a,b): $p > 0.31$ for all analyses). The adjusted analysis retained four interactions: age-by-race, current cigarette smoking-by-occupation, current cigarette smoking-by-race, and lifetime cigarette smoking history-by-race.

Initial dioxin and absolute neutrophils (segs) were not significantly associated in the Model 2 unadjusted analysis (Table 16-16(c): $p=0.151$). A significant interaction between initial dioxin and race was disclosed in the adjusted analysis (Table 16-16(d): $p=0.038$). Results stratified by race are found in Appendix Table L-2-8. After deleting the interaction from the final model, the association between initial dioxin and absolute neutrophils (segs) remained nonsignificant ($p=0.962$). Covariates included in the adjusted analysis were occupation, current cigarette smoking, and lifetime cigarette smoking history. The unadjusted Model 3 analysis revealed a marginally significant difference in mean absolute neutrophils (segs) for high Ranch Hands versus Comparisons (Table 16-16(e): $p=0.063$, Diff. of Mean=0.189). The adjusted mean (adjusted for body fat measures) for the Ranch Hand category was 4.145 thousand/mm^3 compared to only 3.956 thousand/mm^3 for Comparisons. All contrasts were nonsignificant after adjusting for lifetime cigarette smoking history and the age-by-race and current cigarette smoking-by-occupation interactions (Table 16-16(f): $p > 0.68$ for all contrasts).

Results from the Model 4 through 6 unadjusted analysis of absolute neutrophils (segs) were nonsignificant (Table 16-16(g): $p > 0.10$ for all analyses). In each of the adjusted analyses, the interaction of current dioxin and race was significant (Table 16-16(h): $p=0.034$ for Model 4, $p=0.011$ for Model 5, and $p=0.012$ for Model 6). After excluding these interactions from each of the final models, no significant associations between current dioxin and absolute neutrophils (segs) were revealed ($p > 0.45$ for all analyses). Also retained in each adjusted analysis were age, lifetime cigarette smoking history, and the current cigarette smoking-by-occupation interaction. Appendix Table L-2-8 contains results stratified by race for further analysis on the current dioxin interaction. After occupation was removed from the final models, the current dioxin effect became significant in Models 4 and 5 (Appendix Table L-3-10(c): $p=0.029$, Slope=0.0174 for Model 4 and $p=0.036$, Slope=0.0143 for Model 5) and marginally significant in Model 6 ($p=0.068$, Slope=0.0135). These results also reflect the exclusion of the current dioxin-by-race interactions.

Absolute Neutrophils (bands)

Because a substantial number of measurements (372/2,224 or 16.7%) for absolute neutrophils (bands) were equal to 0 counts per mm^3, this variable was analyzed in two forms. A discrete analysis was first performed on the proportion of zero measurements and a second continuous analysis was performed on the nonzero measurements.

Table 16-16.
Analysis of Absolute Neutrophils (segs) (thousand/mm^3)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***946***	***4.012***	***0.062 --***	***0.315***
	Comparison	***1,278***	***3.951***		
Officer	Ranch Hand	364	3.779	0.053 --	0.534
	Comparison	501	3.726		
Enlisted Flyer	Ranch Hand	162	4.119	-0.022 --	0.903
	Comparison	201	4.141		
Enlisted Groundcrew	Ranch Hand	420	4.183	0.094 --	0.320
	Comparison	576	4.089		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	***Ranch Hand***	***945***	***3.568***	***0.025 --***	***0.608***	AGE*RACE (p=0.017)
	Comparison	***1,276***	***3.543***			CSMOK*OCC (p=0.035)
Officer	Ranch Hand	363	3.397	0.044 --	0.561	CSMOK*RACE (p=0.009)
	Comparison	501	3.354			PACKYR*RACE (p=0.047)
Enlisted Flyer	Ranch Hand	162	3.524	-0.084 --	0.490	
	Comparison	201	3.607			
Enlisted Groundcrew	Ranch Hand	420	3.750	0.050 --	0.519	
	Comparison	574	3.700			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-16. (Continued)
Analysis of Absolute Neutrophils (segs) (thousand/mm^3)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	3.910	3.917	0.018	0.0184 (0.0128)	0.151
Medium	172	4.105	4.118			
High	171	4.153	4.132			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	3.573**	0.223	0.0006 (0.0132)**	0.962**	INIT*RACE (p=0.038)
Medium	172	3.540**				OCC (p=0.078)
High	171	3.544**				CSMOK (p<0.001)
						PACKYR (p=0.016)

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of absolute neutrophils (segs) versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-8 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-16. (Continued)
Analysis of Absolute Neutrophils (segs) (thousand/mm^3)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,061	3.957	3.956		
Background RH	371	3.907	3.928	-0.028 --	0.738
Low RH	259	3.947	3.938	-0.018 --	0.848
High RH	258	4.163	4.145	0.189 --	0.063
Low plus High RH	517	4.054	4.041	0.085 --	0.281

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ac]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,059	3.561			PACKYR (p=0.009) AGE*RACE (p=0.015) CSMOK*OCC (p=0.010)
Background RH	370	3.559	-0.002 --	0.974	
Low RH	259	3.578	0.017 --	0.836	
High RH	258	3.595	0.034 --	0.681	
Low plus High RH	517	3.586	0.025 --	0.686	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-16. (Continued)
Analysis of Absolute Neutrophils (segs) (thousand/mm^3)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	3.904 (292)	3.909 (299)	4.167 (297)	0.003	0.0135 (0.0086)	0.116
5	3.889 (297)	3.913 (297)	4.183 (294)	0.003	0.0120 (0.0074)	0.104
6[d]	3.925 (296)	3.917 (297)	4.132 (294)	0.010	0.0069 (0.0079)	0.387

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	3.413** (291)	3.413** (299)	3.516** (297)	0.208	0.0068 (0.0090)**	0.451**	CURR*RACE (p=0.034) AGE (p=0.028) PACKYR (p=0.090) CSMOK*OCC (p=0.014)
5	3.405** (296)	3.423** (297)	3.518** (294)	0.210	0.0051 (0.0076)**	0.498**	CURR*RACE (p=0.011) AGE (p=0.028) PACKYR (p=0.089) CSMOK*OCC (p=0.014)
6[e]	3.413** (295)	3.426** (297)	3.509** (294)	0.209	0.0042 (0.0083)**	0.615**	CURR*RACE (p=0.012) AGE (p=0.033) PACKYR (p=0.098) CSMOK*OCC (p=0.018)

[a] Transformed from natural logarithm scale.
[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.
[c] Slope and standard error based on natural logarithm of absolute neutrophils (segs) versus log_2 (current dioxin + 1).
[d] Adjusted for log_2 total lipids.
[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-8 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

No significant association between group and the proportion of zero measurements for absolute neutrophils (bands) was disclosed in the Model 1 analyses (Table 16-17(a1-b1): $p \geq 0.50$ for all contrasts). Race and current cigarette smoking were significant covariates. The continuous analysis investigating associations between group and nonzero measurements of absolute neutrophils (bands) revealed only one statistically significant difference between Ranch Hands and Comparisons. In the adjusted analysis, the adjusted mean of the absolute neutrophils (bands) for Ranch Hands in the enlisted flyer category was significantly lower than that of the Comparisons (Table 16-17(b2): $p=0.038$, Diff. of Adj. Mean=-0.024). The final model adjusted for age, current cigarette smoking, and the occupation-by-race interaction.

The proportion of zero measurements of absolute neutrophils (bands) did not display a significant association with initial dioxin in the Model 2 analyses (Table 16-17(c1-d1): $p > 0.33$ for unadjusted and adjusted analyses). Race and the initial dioxin-by-lifetime cigarette smoking history interaction ($p=0.018$) were significant in the adjusted analysis. The final adjusted model reflects results after removing the initial dioxin-by-lifetime cigarette smoking history interaction. Appendix Table L-2-9(a) contains additional information on the interaction. No significant relationship between initial dioxin and the nonzero measurements of absolute neutrophils (bands) was disclosed in the unadjusted and adjusted continuous Model 2 analyses (Table 16-17(c2-d2): $p \geq 0.49$ for both analyses). The initial dioxin-by-occupation interaction was significant in the adjusted analysis ($p=0.021$). Results stratified by occupation are found in Appendix Table L-2-9(b). Current cigarette smoking and the interaction of race and occupation also were significant in this analysis.

All unadjusted Model 3 contrasts for zero versus nonzero measurements of absolute neutrophils (bands) were nonsignificant (Table 16-17(e1): $p > 0.58$ for each contrast). In the adjusted analysis, the categorized dioxin-by-lifetime cigarette smoking history interaction was highly significant (Table 16-17(f1): $p < 0.001$). Analyses stratified by each lifetime cigarette smoking history category are presented in Appendix Table L-2-9(c). Race was additionally retained in the adjusted analysis. Nonzero measurements of absolute neutrophils (bands) for Ranch Hands in the four dioxin categories were not significantly different than those of the Comparisons (Table 16-17(e2-f2): $p > 0.82$ for all contrasts). Age and the race-by-occupation and current cigarette smoking-by-race interactions were significant in the final adjusted model.

Current dioxin and the proportion of zero measurements for absolute neutrophils (bands) were not significantly associated in the unadjusted analyses for Models 4, 5, and 6 (Table 16-17(g1): $p > 0.58$ for each analysis). Each adjusted analysis retained race and a highly significant current dioxin-by-lifetime cigarette smoking history interaction (Table 16-17(h1): $p=0.001$ for Model 4, $p=0.003$ for Model 5, and $p=0.002$ for Model 6). Appendix Table L-2-9(d-f) shows results stratified by the levels of lifetime cigarette smoking history. The association between current dioxin and nonzero absolute neutrophils (bands) measurements was nonsignificant in Models 4, 5, and 6 (Table 16-17(g2-h2): $p > 0.18$ for all analyses). Each adjusted analysis retained age, current cigarette smoking, occupation, and race.

Table 16-17.
Analysis of Absolute Neutrophils (bands)
(Zero versus Nonzero)

a1) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Zero	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***946***	***16.9***	***1.02 (0.82,1.28)***	***0.884***
	Comparison	***1,278***	***16.6***		
Officer	Ranch Hand	364	16.2	1.12 (0.77,1.62)	0.629
	Comparison	501	14.8		
Enlisted Flyer	Ranch Hand	162	15.4	0.81 (0.46,1.41)	0.543
	Comparison	201	18.4		
Enlisted Groundcrew	Ranch Hand	420	18.1	1.04 (0.75,1.44)	0.885
	Comparison	576	17.5		

b1) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.03 (0.82,1.29)***	***0.817***	RACE ($p<0.001$) CSMOK ($p=0.055$)
Officer	1.11 (0.76,1.61)	0.587	
Enlisted Flyer	0.82 (0.47,1.44)	0.500	
Enlisted Groundcrew	1.05 (0.75,1.46)	0.791	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-17. (Continued)
Analysis of Absolute Neutrophils (bands) (thousand/mm^3)
(Nonzero Measurements)

a2) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***786***	***0.188***	***0.001 --***	***0.860***
	Comparison	***1,066***	***0.186***		
Officer	Ranch Hand	305	0.190	0.011 --	0.312
	Comparison	427	0.178		
Enlisted Flyer	Ranch Hand	137	0.174	-0.028 --	0.110
	Comparison	164	0.202		
Enlisted Groundcrew	Ranch Hand	344	0.192	0.003 --	0.762
	Comparison	475	0.189		

b2) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	***Ranch Hand***	***786***	***0.169***	***-0.001 --***	0.916	AGE (p=0.003) CSMOK (p<0.001) OCC*RACE (p=0.014)
	Comparison	***1,064***	***0.169***			
Officer	Ranch Hand	305	0.227	0.014 --	0.272	
	Comparison	427	0.213			
Enlisted Flyer	Ranch Hand	137	0.124	-0.024 --	0.038	
	Comparison	164	0.148			
Enlisted Groundcrew	Ranch Hand	344	0.161	0.001 --	0.946	
	Comparison	473	0.160			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-17. (Continued)
Analysis of Absolute Neutrophils (bands)
(Zero versus Nonzero)

c1) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Zero**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	19.5	0.92 (0.76,1.10)	0.332
Medium	172	16.3		
High	171	15.8		

d1) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
517	0.93 (0.78,1.12)**	0.448**	INIT*PACKYR (p=0.018) RACE (p=0.085)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-9 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-17. (Continued)
Analysis of Absolute Neutrophils (bands) (thousand/mm^3)
(Nonzero Measurements)

c2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	140	0.171	0.171	<0.001	0.0035 (0.0304)	0.909
Medium	144	0.203	0.203			
High	144	0.188	0.188			

d2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	140	0.141**	0.140	-0.0228 (0.0330)**	0.490**	INIT*OCC (p=0.021)
Medium	144	0.157**				CSMOK (p<0.001)
High	144	0.144**				RACE*OCC (p=0.021)

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-9 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-17. (Continued)
Analysis of Absolute Neutrophils (bands)
(Zero versus Nonzero)

e1) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Zero	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	16.5		
Background RH	371	17.0	1.05 (0.76,1.44)	0.782
Low RH	259	17.8	1.11 (0.77,1.58)	0.583
High RH	258	16.7	0.99 (0.69,1.44)	0.974
Low plus High RH	517	17.2	1.05 (0.79,1.39)	0.739

f1) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,059			DXCAT*PACKYR (p<0.001) RACE (p<0.001)
Background RH	370	****	****	
Low RH	259	****	****	
High RH	258	****	****	
Low plus High RH	517	****	****	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Categorized dioxin-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table L-2-9 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-17. (Continued)
Analysis of Absolute Neutrophils (bands) (thousand/mm^3)
(Nonzero Measurements)

e2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	886	0.188	0.188		
Background RH	308	0.189	0.189	0.001 --	0.962
Low RH	213	0.188	0.188	0.000 --	0.990
High RH	215	0.186	0.187	-0.001 --	0.905
Low plus High RH	428	0.187	0.187	-0.001 --	0.932

f2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ac]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	884	0.171			AGE (p=0.002) RACE*OCC (p=0.001) CSMOK*RACE (p=0.008)
Background RH	308	0.169	-0.002 --	0.828	
Low RH	213	0.172	0.001 --	0.902	
High RH	215	0.170	-0.001 --	0.927	
Low plus High RH	428	0.171	0.000 --	0.985	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-17. (Continued)
Analysis of Absolute Neutrophils (bands)
(Zero versus Nonzero)

g1) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Zero/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	16.8 (292)	18.7 (299)	15.8 (297)	1.01 (0.90,1.14)	0.876
5	17.9 (297)	18.2 (297)	15.3 (294)	1.00 (0.91,1.11)	0.933
6[c]	17.9 (296)	18.2 (297)	15.3 (294)	1.03 (0.92,1.15)	0.589

h1) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	887	****	****	CURR*PACKYR (p=0.001) RACE (p<0.001)
5	887	****	****	CURR*PACKYR (p=0.003) RACE (p<0.001)
6[d]	886	****	****	CURR*PACKYR (p=0.002) RACE (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

****Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table L-2-9 for further analyses of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 16-17. (Continued)
Analysis of Absolute Neutrophils (bands) (thousand/mm^3)
(Nonzero Measurements)

g2) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	0.192 (243)	0.184 (243)	0.188 (250)	<0.001	-0.0108 (0.0201)	0.592
5	0.192 (244)	0.173 (243)	0.199 (249)	<0.001	-0.0071 (0.0171)	0.679
6[d]	0.197 (243)	0.174 (243)	0.194 (249)	0.008	-0.0246 (0.0185)	0.185

h2) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	0.150 (243)	0.150 (243)	0.155 (250)	0.076	0.0053 (0.0226)	0.814	AGE (p=0.072) CSMOK (p<0.001) OCC (p=0.114) RACE (p=0.003)
5	0.151 (244)	0.143 (243)	0.166 (249)	0.076	0.0052 (0.0188)	0.782	AGE (p=0.073) CSMOK (p<0.001) OCC (p=0.113) RACE (p=0.003)
6[e]	0.154 (243)	0.144 (243)	0.164 (249)	0.079	-0.0078 (0.0207)	0.707	AGE (p=0.093) CSMOK (p<0.001) OCC (p=0.144) RACE (p=0.004)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Absolute Lymphocytes

Model 1 analyses investigating group differences in mean absolute lymphocytes between Ranch Hands and Comparisons did not reveal any significant results (Table 16-18(a,b): $p > 0.36$ for all contrasts). Current cigarette smoking history, occupation, and lifetime cigarette smoking history were retained in the adjusted analysis.

Results from the unadjusted and adjusted Model 2 analysis of absolute lymphocytes were nonsignificant (Table 16-18(c,d): $p > 0.31$ for both analyses). Significant covariates included current cigarette smoking and the age-by-race and the race-by-occupation interactions. All results investigating associations between categorized dioxin and absolute lymphocytes for Model 3 were nonsignificant (Table 16-18(e,f): $p > 0.45$). Lifetime cigarette smoking history and the current cigarette smoking-by-occupation interaction were retained in the final adjusted model.

None of the Model 4 through 6 unadjusted and adjusted analyses revealed significant results (Table 16-18(g,h): $p > 0.38$ for all analyses). Lifetime cigarette smoking and the age-by-race, occupation-by-race, and current cigarette smoking-by-occupation interactions were retained in all adjusted analyses.

Absolute Monocytes

The unadjusted and adjusted Model 1 results for absolute monocytes were nonsignificant (Table 16-19(a,b): $p \geq 0.39$ for all contrasts). The interaction of group and race was significant in the adjusted analysis. Results stratified by race are found in Appendix Table L-2-10. Adjusted results are based on a final model after deletion of this interaction. Additional covariates retained in the adjusted analysis included current cigarette smoking and lifetime cigarette smoking history.

A positive marginally significant association between initial dioxin and absolute monocytes was revealed in the Model 2 unadjusted analysis (Table 16-19(c): $p = 0.069$, Slope$=0.0107$). Adjustment for race, current cigarette smoking, and lifetime cigarette smoking history, however, caused the association to become nonsignificant (Table 16-19(d): $p = 0.104$). Both the unadjusted and adjusted Model 3 analyses revealed marginally significant differences between high Ranch Hands and Comparisons, with high Ranch Hands possessing the greater mean level of absolute monocytes (Table 16-19(e,f): $p = 0.064$, Diff. of Mean$=0.032$ for the unadjusted analysis and $p = 0.079$, Diff. of Adj. Mean$=0.030$ for the adjusted analysis). The remaining unadjusted and adjusted contrasts for Ranch Hands and Comparisons were nonsignificant ($p > 0.26$).

All results from the Model 4, 5, and 6 analyses of absolute monocytes were nonsignificant (Table 16-19(g,h): $p \geq 0.12$ for all analyses). Current cigarette smoking, lifetime cigarette smoking history, and the age-by-race interaction were retained in the adjusted analysis.

Table 16-18.
Analysis of Absolute Lymphocytes (thousand/mm^3)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***946***	***1.937***	***-0.009 --***	***0.771***
	Comparison	***1,278***	***1.946***		
Officer	Ranch Hand	364	1.814	-0.024 --	0.585
	Comparison	501	1.837		
Enlisted Flyer	Ranch Hand	162	1.972	-0.052 --	0.541
	Comparison	201	2.024		
Enlisted Groundcrew	Ranch Hand	420	2.036	0.019 --	0.679
	Comparison	576	2.017		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***945***	***1.934***	***-0.019 --***	0.517	CSMOK ($p<0.001$) OCC ($p<0.001$) PACKYR ($p=0.098$)
	Comparison	***1,276***	***1.953***			
Officer	Ranch Hand	363	1.850	-0.025 --	0.577	
	Comparison	501	1.875			
Enlisted Flyer	Ranch Hand	162	1.931	-0.066 --	0.364	
	Comparison	201	1.997			
Enlisted Groundcrew	Ranch Hand	420	2.008	0.005 --	0.918	
	Comparison	574	2.003			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-18. (Continued)
Analysis of Absolute Lymphocytes (thousand/mm^3)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	1.870	1.874	0.006	0.0129 (0.0129)	0.318
Medium	172	1.952	1.952			
High	171	1.990	1.986			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	1.782	0.094	0.0041 (0.0144)	0.773	CSMOK ($p<0.001$)
Medium	172	1.790				AGE*RACE ($p=0.017$)
High	171	1.823				RACE*OCC ($p=0.009$)

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of absolute lymphocytes versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-18. (Continued)
Analysis of Absolute Lymphocytes (thousand/mm^3)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,061	1.931	1.930		
Background RH	371	1.905	1.909	-0.021 --	0.608
Low RH	259	1.907	1.909	-0.021 --	0.660
High RH	258	1.966	1.960	0.030 --	0.539
Low plus High RH	517	1.936	1.934	0.004 --	0.911

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,059	1.931			PACKYR (p=0.114) CSMOK*OCC (p=0.036)
Background RH	370	1.932	0.001 --	0.970	
Low RH	259	1.910	-0.021 --	0.662	
High RH	258	1.897	-0.034 --	0.484	
Low plus High RH	517	1.904	-0.027 --	0.459	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-18. (Continued)
Analysis of Absolute Lymphocytes (thousand/mm^3)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	1.890 (292)	1.929 (299)	1.950 (297)	<0.001	0.0052 (0.0086)	0.549
5	1.882 (297)	1.934 (297)	1.954 (294)	0.001	0.0055 (0.0074)	0.461
6[d]	1.900 (296)	1.936 (297)	1.931 (294)	0.006	0.0006 (0.0080)	0.939

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	1.855 (291)	1.868 (299)	1.799 (297)	0.115	-0.0061 (0.0095)	0.524	PACKYR (p=0.083) AGE*RACE (p=0.006) OCC*RACE (p=0.020) CSMOK*OCC (p=0.011)
5	1.845 (296)	1.867 (297)	1.809 (294)	0.115	-0.0035 (0.0080)	0.660	PACKYR (p=0.081) AGE*RACE (p=0.007) OCC*RACE (p=0.020) CSMOK*OCC (p=0.010)
6[e]	1.865 (295)	1.874 (297)	1.794 (294)	0.116	-0.0075 (0.0087)	0.388	PACKYR (p=0.103) AGE*RACE (p=0.006) OCC*RACE (p=0.019) CSMOK*OCC (p=0.015)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of absolute lymphocytes versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 16-19.
Analysis of Absolute Monocytes (thousand/mm^3)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***946***	***0.462***	***0.009 --***	***0.390***
	Comparison	***1,278***	***0.453***		
Officer	Ranch Hand	364	0.461	0.014 --	0.416
	Comparison	501	0.447		
Enlisted Flyer	Ranch Hand	162	0.456	-0.003 --	0.900
	Comparison	201	0.459		
Enlisted Groundcrew	Ranch Hand	420	0.466	0.009 --	0.549
	Comparison	576	0.457		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***945***	***0.450*****	***0.006 --*****	0.527**	GROUP*RACE (p=0.034)
	Comparison	***1,276***	***0.444*****			CSMOK (p<0.001)
Officer	Ranch Hand	363	0.459**	0.013 --**	0.426**	PACKYR (p=0.081)
	Comparison	501	0.446**			
Enlisted Flyer	Ranch Hand	162	0.435**	-0.007 --**	0.780**	
	Comparison	201	0.442**			
Enlisted Groundcrew	Ranch Hand	420	0.451**	0.006 --**	0.696**	
	Comparison	574	0.445**			

[a] Transformed from the square root scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

[c] P-values based on difference of means on square root scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-10 for further analysis of this interaction.

Table 16-19. (Continued)
Analysis of Absolute Monocytes (thousand/mm^3)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	0.439	0.441	0.014	0.0107 (0.0059)	0.069
Medium	172	0.471	0.472			
High	171	0.486	0.482			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	0.414	0.066	0.0094 (0.0058)	0.104	CSMOK (p=0.006)
Medium	172	0.430				PACKYR (p=0.017)
High	171	0.449				RACE (p=0.054)

[a] Transformed from square root scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on square root of absolute monocytes versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-19. (Continued)
Analysis of Absolute Monocytes (thousand/mm^3)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,061	0.448	0.448		
Background RH	371	0.459	0.462	0.014 --	0.348
Low RH	259	0.447	0.446	-0.002 --	0.895
High RH	258	0.482	0.480	0.032 --	0.064
Low plus High RH	517	0.465	0.463	0.015 --	0.266

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,059	0.449			AGE (p=0.107)
Background RH	370	0.461	0.012 --	0.430	CSMOK (p<0.001)
Low RH	259	0.445	-0.004 --	0.789	PACKYR (p=0.025)
High RH	258	0.479	0.030 --	0.079	
Low plus High RH	517	0.462	0.013 --	0.332	

[a] Transformed from square root scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on square root scale.

[d] P-value is based on difference of means on square root scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-19. (Continued)
Analysis of Absolute Monocytes (thousand/mm^3)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	0.461 (292)	0.442 (299)	0.484 (297)	0.002	0.0054 (0.0041)	0.191
5	0.462 (297)	0.438 (297)	0.488 (294)	0.002	0.0046 (0.0035)	0.190
6[d]	0.463 (296)	0.438 (297)	0.488 (294)	0.002	0.0040 (0.0038)	0.297

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	0.446 (291)	0.428 (299)	0.470 (297)	0.047	0.0065 (0.0041)	0.120	CSMOK (p=0.001) PACKYR (p=0.023) AGE*RACE (p=0.015)
5	0.449 (296)	0.425 (297)	0.474 (294)	0.047	0.0053 (0.0035)	0.134	CSMOK (p=0.001) PACKYR (p=0.023) AGE*RACE (p=0.014)
6[e]	0.446 (295)	0.423 (297)	0.476 (294)	0.048	0.0058 (0.0038)	0.133	CSMOK (p=0.001) PACKYR (p=0.020) AGE*RACE (p=0.016)

[a] Transformed from square root scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on square root of absolute monocytes versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Absolute Eosinophils

A sizable number of absolute eosinophil measurements collected at the laboratory examination were equal to 0 counts per mm^3 (259/2,224 or 11.6%). Consequently, this variable was analyzed in two ways. First, the proportion of zero measurements was analyzed for associations with exposure in a discrete analysis and secondly, nonzero measurements were investigated for an association with exposure in a continuous analysis.

In the Model 1 unadjusted analysis of zero versus nonzero measurements of absolute eosinophils, a significant overall difference between Ranch Hands and Comparisons was disclosed (Table 16-20(a1): $p=0.050$, Est. RR=0.76). A larger percentage of Comparisons possessed zero-valued measurements than Ranch Hands (12.8% vs. 10.0%). Analyses stratified by occupation revealed similar results in the officer category ($p=0.018$, Est. RR=0.59), where 15.0% of absolute eosinophil measurements for Comparisons equaled zero in contrast to only 9.3% for Ranch Hands. Contrasts in the enlisted flyer and enlisted groundcrew categories were nonsignificant ($p>0.29$). Results were identical in the adjusted analysis because no covariates were retained in the final model. In the continuous analyses of the nonzero-valued measurements for absolute eosinophils, no significant differences between Ranch Hands and Comparisons were observed (Table 16-20(a2-b2): $p>0.13$ for each analysis). Race, current cigarette smoking, and the age-by-lifetime cigarette smoking history interaction were significant.

The Model 2 analyses of the proportion of zero measurements for absolute eosinophils found no significant associations with initial dioxin (Table 16-20(c1-d1): $p>0.62$). Two significant initial dioxin interactions involving age and occupation were retained in the adjusted analysis ($p=0.026$ and $p<0.001$ respectively). Stratified results for each interaction are located in Appendix Table L-2-11(a-b). The final model also adjusted for race. Model 2 analyses on the nonzero measurements of absolute eosinophils also found no significant associations with initial dioxin (Table 16-20(c2-d2): $p\geq 0.89$). Current cigarette smoking was retained in the final model.

The proportion of zero measurements was not significantly different between Ranch Hands and Comparisons in the Model 3 analyses of absolute eosinophils (Table 16-20(e1-f1): $p>0.27$ for each contrast). The age-by-current cigarette smoking interaction was retained in the adjusted analysis. The Model 3 adjusted analysis of the nonzero measurements of absolute eosinophils revealed a marginally significant negative difference between the low plus high Ranch Hand category and Comparisons (Table 16-20(f2): $p=0.098$, Diff. of Adj. Mean=-0.011). The remaining unadjusted and adjusted contrasts were nonsignificant (Table 16-20(e2-f2): $p>0.10$ for each contrast). Race, current cigarette smoking, and lifetime cigarette smoking history were retained in the adjusted analysis.

The unadjusted Model 4 analysis of zero versus nonzero measurements of absolute eosinophils revealed no significant association with current dioxin (Table 16-20(g1): $p=0.116$). Adjustment for the race-by-current cigarette smoking interaction led to a marginally significant positive association (Table 16-20(h1): $p=0.082$, Adj. RR=1.14). Marginally significant associations between the proportion of zero absolute eosinophil measurements and current dioxin also were observed in both the unadjusted and adjusted

Table 16-20.
Analysis of Absolute Eosinophils
(Zero versus Nonzero)

a1) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Zero	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***946***	***10.0***	***0.76 (0.58,0.99)***	***0.050***
	Comparison	***1,278***	***12.8***		
Officer	Ranch Hand	364	9.3	0.59 (0.38,0.90)	0.018
	Comparison	501	15.0		
Enlisted Flyer	Ranch Hand	162	8.0	0.64 (0.32,1.31)	0.293
	Comparison	201	11.9		
Enlisted Groundcrew	Ranch Hand	420	11.4	1.01 (0.68,1.51)	0.999
	Comparison	576	11.3		

b1) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
All	***0.76 (0.58,0.99)***	***0.050***	
Officer	0.59 (0.38,0.90)	0.018	
Enlisted Flyer	0.64 (0.32,1.31)	0.293	
Enlisted Groundcrew	1.01 (0.68,1.51)	0.999	

Table 16-20. (Continued)
Analysis of Absolute Eosinophils (thousand/mm^3)
(Nonzero Measurements)

a2) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***851***	***0.169***	***-0.004 --***	***0.502***
	Comparison	***1,114***	***0.172***		
Officer	Ranch Hand	330	0.167	-0.003 --	0.720
	Comparison	426	0.170		
Enlisted Flyer	Ranch Hand	149	0.163	-0.018 --	0.200
	Comparison	177	0.182		
Enlisted Groundcrew	Ranch Hand	372	0.172	0.001 --	0.873
	Comparison	511	0.171		

b2) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***850***	***0.158***	***-0.004 --***	0.373	RACE (p=0.026) CSMOK (p<0.001) AGE*PACKYR (p=0.034)
	Comparison	***1,112***	***0.162***			
Officer	Ranch Hand	329	0.159	-0.004 --	0.661	
	Comparison	426	0.162			
Enlisted Flyer	Ranch Hand	149	0.149	-0.018 --	0.133	
	Comparison	177	0.168			
Enlisted Groundcrew	Ranch Hand	372	0.160	0.000 --	0.999	
	Comparison	509	0.160			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-20. (Continued)
Analysis of Absolute Eosinophils
(Zero versus Nonzero)

c1) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Zero**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	11.5	1.05 (0.86,1.29)	0.625
Medium	172	11.1		
High	171	9.9		

d1) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
517	1.04 (0.82,1.31)**	0.769**	INIT*AGE (p=0.026) INIT*OCC (p<0.001) RACE (p=0.080)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table L-2-11 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-20. (Continued)
Analysis of Absolute Eosinophils (thousand/mm^3)
(Nonzero Measurements)

c2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	154	0.163	0.163	0.006	0.0036 (0.0271)	0.894
Medium	153	0.167	0.167			
High	154	0.158	0.158			

d2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	154	0.166	0.041	-0.0037 (0.0267)	0.890	CSMOK ($p < 0.001$)
Medium	153	0.165				
High	154	0.157				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of absolute eosinophils versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-20. (Continued)
Analysis of Absolute Eosinophils
(Zero versus Nonzero)

e1) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Zero	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	11.8		
Background RH	371	9.2	0.81 (0.54,1.21)	0.305
Low RH	259	11.2	0.90 (0.59,1.39)	0.643
High RH	258	10.5	0.83 (0.53,1.29)	0.409
Low plus High RH	517	10.8	0.87 (0.62,1.21)	0.404

f1) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,059			AGE*CSMOK (p=0.014)
Background RH	371	0.80 (0.53,1.20)	0.276	
Low RH	259	0.91 (0.59,1.40)	0.653	
High RH	258	0.83 (0.53,1.29)	0.400	
Low plus High RH	517	0.87 (0.62,1.21)	0.401	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-20. (Continued)
Analysis of Absolute Eosinophils (thousand/mm^3)
(Nonzero Measurements)

e2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	936	0.173	0.173		
Background RH	337	0.175	0.175	0.002 --	0.785
Low RH	230	0.165	0.164	-0.009 --	0.316
High RH	231	0.161	0.161	-0.012 --	0.171
Low plus High RH	461	0.163	0.163	-0.010 --	0.126

f2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	934	0.162			RACE (p=0.034) CSMOK (p<0.001) PACKYR (p=0.100)
Background RH	336	0.164	0.002 --	0.797	
Low RH	230	0.154	-0.008 --	0.354	
High RH	231	0.149	-0.013 --	0.103	
Low plus High RH	461	0.151	-0.011 --	0.098	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-20. (Continued)
Analysis of Absolute Eosinophils
(Zero versus Nonzero)

g1) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Zero/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	9.6 (292)	10.0 (299)	10.8 (297)	1.13 (0.97,1.30)	0.116
5	9.4 (297)	10.4 (297)	10.5 (294)	1.12 (0.98,1.27)	0.085
6[c]	9.5 (296)	10.4 (297)	10.5 (294)	1.11 (0.97,1.27)	0.144

h1) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	888	1.14 (0.99,1.32)	0.082	RACE*CSMOK (p=0.014)
5	888	1.13 (0.99,1.28)	0.065	RACE*CSMOK (p=0.015)
6[d]	887	1.12 (0.96,1.32)**	0.155**	CURR*OCC (p=0.043) RACE*CSMOK (p=0.026)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-11 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 16-20. (Continued)
Analysis of Absolute Eosinophils (thousand/mm^3)
(Nonzero Measurements)

g2) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	0.174 (264)	0.167 (269)	0.163 (265)	0.002	-0.0243 (0.0181)	0.180
5	0.173 (269)	0.170 (266)	0.161 (263)	0.002	-0.0206 (0.0154)	0.182
6[d]	0.174 (268)	0.171 (266)	0.159 (263)	0.003	-0.0264 (0.0166)	0.113

h2) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	0.160 (263)	0.153 (269)	0.149 (265)	0.046	-0.0221 (0.0178)	0.213	RACE (p=0.060) CSMOK (p<0.001) PACKYR (p=0.044)
5	0.159 (268)	0.156 (266)	0.146 (263)	0.046	-0.0191 (0.0151)	0.205	RACE (p=0.058) CSMOK (p<0.001) PACKYR (p=0.042)
6[e]	0.159 (267)	0.156 (266)	0.146 (263)	0.046	-0.0212 (0.0164)	0.197	RACE (p=0.063) CSMOK (p<0.001) PACKYR (p=0.048)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of absolute eosinophils versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

analyses for Model 5 (Table 16-20(g1-h1): p=0.085, Est. RR=1.12 and p=0.065, Adj. RR=1.13 respectively). The final model included the race-by-current cigarette smoking interaction. No significant associations with current dioxin were disclosed in the Model 6 analyses ($p>0.14$). The adjusted analysis retained the current dioxin-by-occupation interaction (p=0.043). Results stratified by occupation are presented in Appendix Table L-2-11(c). When occupation was removed from this model, a marginally significant association between the proportion of zero measurements and current dioxin was observed (Table L-3-13: p=0.095, Adj. RR=1.13). In Models 4 through 6, all results from the continuous analyses of the nonzero measurements of absolute eosinophils were nonsignificant (Table 16-20(g2-h2): $p>0.11$ for all analyses). Each final model adjusted for race, current cigarette smoking, and lifetime cigarette smoking history.

Absolute Basophils

Comparable to absolute neutrophils (bands) and absolute eosinophils, the substantial number of measurements equal to 0 thousand/mm^3 for absolute basophils (1,005/2,224 or 45.2%) necessitated two types of analyses: a discrete analysis on the proportion of zero measurements and a continuous analysis on the nonzero measurements.

No significant results were found in the Model 1 analyses investigating associations between group and the proportion of zero measurements for absolute basophils (Table 16-21(a1-b1): $p\geq0.58$ for all analyses). Age, current cigarette smoking, and the race-by-lifetime cigarette smoking history interaction were retained in the final adjusted model. Model 1 results from the continuous unadjusted analysis of nonzero measurements for absolute basophils were nonsignificant (Table 16-21(a2): $p>0.18$). In the adjusted analysis based on nonzero measurements, Ranch Hands in the enlisted flyer category possessed a marginally significant lower mean level of absolute basophils than Comparisons (Table 16-21(b2): p=0.094, Diff. of Adj. Means=-0.008). Race and current cigarette smoking were significant in the final adjusted model.

The Model 2 analyses examining zero versus nonzero measurements of absolute basophils revealed nonsignificant results (Table 16-21(c1-d1): $p>0.66$). The adjusted analysis duplicated the unadjusted analysis because no covariates were retained in the final model. The unadjusted Model 2 analysis of absolute basophil measurements greater than 0 thousand/mm^3 disclosed a significant positive association with initial dioxin (Table 16-21(c2): p=0.037, Slope=0.0429). After adjusting for current cigarette smoking, the association with initial dioxin was marginally significant (Table 16-21(d2): p=0.092, slope=0.0334).

All results from the Model 3 analyses of zero versus nonzero measurements of absolute basophils were nonsignificant (Table 16-21(e1-f1): $p\geq0.53$ for all analyses). Current cigarette smoking was retained in the adjusted analysis. Similarly, Model 3 continuous analyses on the nonzero measurements of absolute basophils were nonsignificant (Table 16-21(e2-f2): $p>0.26$ for all analyses). Race, current cigarette smoking, and lifetime cigarette smoking history were retained.

The proportion of zero measurements for absolute basophils did not display a significant association with current dioxin in the Model 4, 5, and 6 unadjusted analyses (Table

Table 16-21.
Analysis of Absolute Basophils
(Zero versus Nonzero)

a1) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Zero**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***946***	***45.0***	***0.99 (0.84,1.17)***	***0.932***
	Comparison	***1,278***	***45.3***		
Officer	Ranch Hand	364	44.0	0.95 (0.72,1.24)	0.744
	Comparison	501	45.3		
Enlisted Flyer	Ranch Hand	162	43.2	0.92 (0.61,1.40)	0.774
	Comparison	201	45.3		
Enlisted Groundcrew	Ranch Hand	420	46.7	1.06 (0.82,1.36)	0.719
	Comparison	576	45.3		

b1) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.99 (0.83,1.17)***	***0.875***	AGE (p=0.065)
Officer	0.95 (0.72,1.25)	0.713	CSMOK (p=0.011)
Enlisted Flyer	0.89 (0.58,1.35)	0.580	RACE*PACKYR (p=0.012)
Enlisted Groundcrew	1.06 (0.82,1.36)	0.672	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-21. (Continued)
Analysis of Absolute Basophils (thousand/mm^3)
(Nonzero Measurements)

a2) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***520***	***0.091***	***0.002 --***	***0.500***
	Comparison	***699***	***0.089***		
Officer	Ranch Hand	204	0.088	0.003 --	0.348
	Comparison	274	0.085		
Enlisted Flyer	Ranch Hand	92	0.089	-0.008 --	0.186
	Comparison	110	0.097		
Enlisted Groundcrew	Ranch Hand	224	0.093	0.003 --	0.318
	Comparison	315	0.090		

b2) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***520***	***0.085***	***0.001 --***	***0.653***	RACE (p=0.011)
	Comparison	***698***	***0.084***			CSMOK (p<0.001)
Officer	Ranch Hand	204	0.083	0.003 --	0.360	
	Comparison	274	0.080			
Enlisted Flyer	Ranch Hand	92	0.081	-0.008 --	0.094	
	Comparison	110	0.089			
Enlisted Groundcrew	Ranch Hand	224	0.086	0.003 --	0.386	
	Comparison	314	0.083			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 16-21. (Continued)
Analysis of Absolute Basophils
(Zero versus Nonzero)

c1) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Zero**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	174	45.4	0.97 (0.85,1.11)	0.669
Medium	172	41.3		
High	171	46.8		

d1) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
517	0.97 (0.85,1.11)	0.669	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-21. (Continued)
Analysis of Absolute Basophils (thousand/mm^3)
(Nonzero Measurements)

c2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	95	0.084	0.084	0.016	0.0429 (0.0204)	0.037
Medium	101	0.087	0.087			
High	91	0.095	0.095			

d2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	95	0.086	0.093	0.0334 (0.0197)	0.092	CSMOK ($p < 0.001$)
Medium	101	0.087				
High	91	0.094				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of absolute basophils versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 16-21. (Continued)
Analysis of Absolute Basophils
(Zero versus Nonzero)

e1) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Zero	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	46.1		
Background RH	371	45.8	0.98 (0.77,1.25)	0.876
Low RH	259	44.4	0.93 (0.70,1.22)	0.587
High RH	258	44.6	0.95 (0.72,1.25)	0.725
Low plus High RH	517	44.5	0.94 (0.76,1.16)	0.561

f1) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,059			CSMOK (p=0.042)
Background RH	371	0.98 (0.77,1.25)	0.869	
Low RH	259	0.93 (0.71,1.22)	0.595	
High RH	258	0.94 (0.71,1.24)	0.659	
Low plus High RH	517	0.93 (0.76,1.16)	0.530	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-21. (Continued)
Analysis of Absolute Basophils (thousand/mm^3)
(Nonzero Measurements)

e2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	572	0.089	0.089		
Background RH	201	0.091	0.092	0.003 --	0.370
Low RH	144	0.085	0.085	-0.004 --	0.262
High RH	143	0.093	0.092	0.003 --	0.333
Low plus High RH	287	0.089	0.088	-0.001 --	0.918

f2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	571	0.084			RACE (p=0.057) CSMOK (p<0.001) PACKYR (p=0.117)
Background RH	200	0.087	0.003 --	0.304	
Low RH	144	0.081	-0.003 --	0.316	
High RH	143	0.086	0.002 --	0.653	
Low plus High RH	287	0.083	-0.001 --	0.719	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 16-21. (Continued)
Analysis of Absolute Basophils
(Zero versus Nonzero)

g1) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Zero/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	44.5 (292)	46.5 (299)	44.1 (297)	0.98 (0.90,1.08)	0.715
5	44.4 (297)	46.8 (297)	43.9 (294)	0.99 (0.91,1.07)	0.767
6[c]	44.3 (296)	46.8 (297)	43.9 (294)	0.98 (0.90,1.07)	0.673

h1) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	888	0.98 (0.90,1.08)	0.715	
5	888	0.99 (0.91,1.07)	0.767	
6[c]	887	0.98 (0.90,1.07)	0.673	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 16-21. (Continued)
Analysis of Absolute Basophils (thousand/mm^3)
(Nonzero Measurements)

g2) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	0.090 (162)	0.087 (160)	0.091 (166)	<0.001	0.0056 (0.0143)	0.695
5	0.089 (165)	0.087 (158)	0.093 (165)	<0.001	0.0060 (0.0123)	0.624
6[d]	0.091 (165)	0.087 (158)	0.091 (165)	0.013	-0.0062 (0.0132)	0.640

h2) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	0.083 (162)	0.081 (160)	0.082 (166)	0.067	0.0014 (0.0139)	0.921	RACE (p=0.014) CSMOK (p<0.001)
5	0.081** (165)	0.081** (158)	0.083** (165)	0.077	0.0020 (0.0119)**	0.869**	CURR*RACE (p=0.023) CSMOK (p<0.001)
6[e]	0.083** (165)	0.082** (158)	0.082** (165)	0.086	-0.0079 (0.0128)**	0.537**	CURR*RACE (p=0.019) CSMOK (p<0.001)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of absolute basophils versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table L-2-12 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

16-21(g1): $p>0.67$). The adjusted analysis was identical to the unadjusted analysis because no covariates were retained in the final model. All results from the Model 4, 5, and 6 continuous analyses of nonzero measurements for absolute basophils were nonsignificant (Table 16-21(g2-h2): $p>0.53$ for all analyses). The Model 5 and Model 6 adjusted analyses retained a significant interaction between current dioxin and race. Appendix Table L-2-12 shows results from these two models stratified by race. Current cigarette smoking was retained in all three adjusted analyses, and race was additionally retained in the Model 4 analysis.

Longitudinal Analysis

Laboratory Examination Variables

Longitudinal analyses were conducted on platelet count, both in the continuous form and discretized as abnormally high versus normal and abnormal low combined. The purpose of these analyses were to examine whether changes over time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Models 4, 5, and 6 were not examined in the longitudinal analyses because current dioxin is the measure of exposure in these models. Current dioxin changes over time and is not available for all participants for 1982 and 1992.

Longitudinal analyses for the continuous form of platelet count examined the paired difference between the measurements from 1982 and 1992. These paired differences measured the change in the ratio over time. Each of the three models used in the longitudinal analysis was adjusted for age and the platelet count measured in 1982. The analyses of Models 2 and 3 also were adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

For the discretized longitudinal analysis of platelet count, relative risks at the 1992 examination were examined for participants who were classified as "normal" or "abnormal low" at the 1982 examination. Participants classified as "abnormal" at the 1982 examination were excluded because the focus of the analyses was on investigating the temporal effects of dioxin during the period between 1982 and 1992. Participants classified as "abnormal" in 1982 already were abnormal before this period; consequently, only participants classified as "normal" or "abnormal low" at the 1982 examination were considered to be at risk when the effects of dioxin over time were explored. The rate of abnormalities under this restriction approximates an incidence rate between 1982 and 1992. All three models were adjusted for age; Models 2 and 3 also were adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Platelet Count (Continuous)

Platelet count group differences of examination mean change (from 1982 to 1992) overall and within the enlisted flyer and enlisted groundcrew strata were nonsignificant (Table 16-22(a): $p>0.44$ for each analysis). The officer stratum displayed a marginally

Table 16-22.
Longitudinal Analysis of Platelet Count (thousand/mm^3)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***273.9 (891)***	***268.1 (866)***	***261.1 (859)***	***250.7 (891)***	***-23.1***	***-5.2***	***0.444***
	Comparison	***262.9 (1,058)***	***264.4 (1,033)***	***255.4 (1,027)***	***244.9 (1,058)***	***-18.0***		
Officer	Ranch Hand	263.0 (335)	258.8 (328)	253.6 (328)	238.9 (335)	-24.1	-7.1	0.068
	Comparison	258.2 (401)	262.5 (393)	252.7 (387)	241.1 (401)	-17.1		
Enlisted Flyer	Ranch Hand	281.8 (158)	272.6 (156)	265.2 (153)	256.0 (158)	-25.9	-4.5	0.576
	Comparison	261.8 (174)	257.0 (171)	246.6 (172)	240.5 (174)	-21.4		
Enlisted Groundcrew	Ranch Hand	280.0 (398)	274.4 (382)	266.0 (378)	258.8 (398)	-21.2	-3.7	0.830
	Comparison	267.1 (483)	268.6 (469)	260.8 (468)	249.6 (483)	-17.5		

[a] Transformed from square root scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of square root of platelet count; results adjusted for square root of platelet count in 1982 and age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 16-22. (Continued)
Longitudinal Analysis of Platelet Count (thousand/mm^3)
(Continuous)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
	Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination					
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	264.6 (167)	263.5 (163)	254.7 (165)	245.2 (167)	0.0224 (0.0442)	0.612
Medium	281.3 (168)	271.3 (162)	266.9 (164)	253.0 (168)		
High	279.3 (165)	271.9 (162)	266.1 (159)	258.3 (165)		

[a] Transformed from square root scale.

[b] Results based on difference between square root of platelet count in 1992 and square root of platelet count in 1982 versus log_2 (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, square root of 1982 platelet count, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 16-22. (Continued)
Longitudinal Analysis of Platelet Count (thousand/mm^3)
(Continuous)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean[a]/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	261.6 (912)	263.4 (899)	254.4 (898)	244.4 (912)	-17.2		
Background RH	271.0 (337)	266.3 (333)	259.2 (331)	246.9 (337)	-24.1	-7.0	0.097
Low RH	268.4 (249)	264.4 (242)	257.1 (246)	245.6 (249)	-22.8	-5.6	0.510
High RH	281.7 (251)	273.3 (245)	268.0 (242)	258.7 (251)	-23.0	-5.8	0.755
Low plus High RH	275.0 (500)	268.9 (487)	262.5 (488)	252.1 (500)	-22.9	-5.7	0.819

[a] Transformed from square root scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of square root of platelet count; results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, square root of platelet count in 1982, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin $>$10 ppt, 10 ppt $<$ Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin $>$10 ppt, Initial Dioxin $>$143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

significant difference of examination mean change between Ranch Hands and Comparisons ($p=0.068$, Diff. of Exam. Mean Change= -7.1).

The Model 2 longitudinal analysis of platelet count in continuous form was not significant (Table 16-22(b): $p=0.612$). For Model 3, the difference of examination mean change between background Ranch Hands and Comparisons was marginally significant (Table 16-22(c): $p=0.097$, Diff. of Exam. Mean Change= -7.0). The background Ranch Hands exhibited a larger decrease in platelet count means from 1982 to 1992 than Comparisons. The remaining Model 3 contrasts were not significant (Table 16-22(c): $p \geq 0.51$ for each analysis).

Platelet Count (Discrete)

The longitudinal analysis of platelet count in discrete form was conditioned on participants who had either low or normal platelet counts in 1982. The longitudinal analysis for Model 1 did not detect a significant difference between Ranch Hands and Comparisons in the percentage of participants with normal or low platelet counts in 1982 and abnormally high platelet counts in 1992 (Table 16-23(a): $p > 0.52$ for all analyses).

Model 2 did not show a significant relationship between initial dioxin and abnormally high platelet counts in 1992, conditioned on normal or low platelet counts in 1982 (Table 16-23(b): $p=0.272$).

The Model 3 longitudinal analysis of abnormally high platelet counts detected a marginally significant relative risk for the high Ranch Hand category (Table 16-23(c): $p=0.072$, Adj. RR=3.24). Among Ranch Hands in the high dioxin category with either low or normal platelet counts during the 1982 examination, 2.0 percent had abnormally high platelet counts in 1992, while only 0.6 percent of Comparisons with either low or normal platelet counts during the 1982 examination had abnormally high platelet counts at the 1992 examination. The remaining contrasts in Model 3 were nonsignificant ($p > 0.25$).

DISCUSSION

The variables analyzed in this chapter serve as indices of the three peripheral blood lines (erythrocytes, leukocytes, and platelets). These variables are heavily relied upon to reflect disease of the hematopoietic system and also to alert the clinician to the presence of disease in other organ systems. The total WBC count varies across a broad range of disease states. Though lacking specificity, leukocytosis or leukopenia can serve as a sensitive clue to the presence of a host of infections, inflammatory and neoplastic disorders, and can point to the need for further investigation.

As elements essential to normal coagulation, the platelets have a short half-life and are most subject to decreased survival in the presence of a wide range of diseases, toxic chemical exposure, and numerous prescription and over-the-counter medications. The normal range ($130,000/mm^3$ to $400,000/mm^3$) allows subtle changes in platelet survival to occur and not be identified as abnormal. Furthermore, small differences in the total platelet count do not have a clinically significant effect on clotting mechanisms.

Table 16-23.
Longitudinal Analysis of Platelet Count
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Percent Abnormal High/(n) Examination			
		1982	1985	1987	1992
All	***Ranch Hand***	***0.8 (891)***	***1.8 (866)***	***2.2 (859)***	***1.2 (891)***
	Comparison	***1.0 (1,058)***	***1.6 (1,033)***	***1.5 (1,027)***	***1.0 (1,058)***
Officer	Ranch Hand	0.6 (335)	2.1 (328)	1.8 (328)	0.3 (335)
	Comparison	0.5 (401)	1.0 (393)	1.3 (387)	0.7 (401)
Enlisted Flyer	Ranch Hand	0.6 (158)	1.9 (156)	3.3 (153)	1.3 (158)
	Comparison	1.7 (174)	1.8 (171)	0.6 (172)	1.1 (174)
Enlisted Groundcrew	Ranch Hand	1.0 (398)	1.6 (382)	2.1 (378)	2.0 (398)
	Comparison	1.0 (483)	2.1 (469)	1.9 (468)	1.0 (483)

Occupational Category	Group	Abnormal Low or Normal in 1982			
		n in 1992	Percent Abnormal High in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***884***	***0.8***	***1.18 (0.41,3.39)***	***0.752***
	Comparison	***1,048***	***0.7***		
Officer	Ranch Hand	333	0.0	--	--
	Comparison	399	0.5		
Enlisted Flyer	Ranch Hand	157	1.3	2.19 (0.20,24.45)	0.523
	Comparison	171	0.6		
Enlisted Groundcrew	Ranch Hand	394	1.3	1.53 (0.41,5.69)	0.529
	Comparison	478	0.8		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had abnormal low or normal platelet counts in 1982 (see Chapter 7, Statistical Methods).

Table 16-23. (Continued)
Longitudinal Analysis of Platelet Count
(Discrete)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent Abnormal High/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	0.6 (167)	1.2 (163)	2.4 (165)	0.6 (167)
Medium	0.6 (168)	1.2 (162)	3.1 (164)	1.8 (168)
High	0.6 (165)	1.9 (162)	2.5 (159)	3.0 (165)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Abnormal Low or Normal in 1982			
Initial Dioxin	n in 1992	Percent Abnormal High in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	166	0.0	1.41 (0.77,2.57)	0.272
Medium	167	1.2		
High	164	2.4		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had abnormal low or normal platelet counts in 1982 (see Chapter 7, Statistical Methods).

Table 16-23. (Continued)
Longitudinal Analysis of Platelet Count
(Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
Dioxin Category	Percent Abnormal High/(n) Examination			
	1982	1985	1987	1992
Comparison	0.9 (912)	1.6 (899)	1.3 (898)	0.8 (912)
Background RH	1.2 (337)	2.1 (333)	1.8 (331)	0.3 (337)
Low RH	0.4 (249)	1.2 (242)	2.0 (246)	0.8 (249)
High RH	0.8 (251)	1.6 (245)	3.3 (242)	2.8 (251)
Low plus High RH	0.6 (500)	1.4 (487)	2.7 (488)	1.8 (500)

Dioxin Category	Abnormal Low or Normal in 1982			
	n in 1992	Percent Abnormal High in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	904	0.6		
Background RH	333	0.0	--	--
Low RH	248	0.4	0.71 (0.08,6.15)	0.755
High RH	249	2.0	3.24 (0.90,11.70)	0.072
Low plus High RH	497	1.2	2.00 (0.60,6.66)	0.258

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin $>$10 ppt, 10 ppt $<$ Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin $>$10 ppt, Initial Dioxin $>$ 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had abnormal low or normal platelet counts in 1982 (see Chapter 7, Statistical Methods).

Of the 13 laboratory variables examined, only the analyses of the platelet count yielded significant positive results. In the enlisted flyer and enlisted groundcrew occupational categories, mean platelet counts in continuous (but not discrete) form were significantly higher in Ranch Hands than in Comparisons; though the difference in the means (14,100/mm^3 and 9,200/mm^3 for enlisted flyers and enlisted groundcrew respectively) cannot be considered clinically significant.

Very few of the serum dioxin analyses yielded significant results. By both unadjusted and adjusted analysis, Ranch Hands with high extrapolated initial levels of serum dioxin had significantly higher mean platelet counts than Comparisons. In the unadjusted continuous analyses of the three models employing current serum dioxin and in a pattern consistent with a positive dose-response, mean platelet counts were increased in Ranch Hands with higher levels of serum dioxin. When adjusted for covariates, however, the findings were no longer significant. In the unadjusted discrete analyses, Ranch Hands with the highest levels of current serum dioxin were most at risk for an elevated platelet count and in Model 4 (lipid-adjusted current dioxin), the findings remained significant after adjustment for covariates. Although of uncertain biologic significance, these results are consistent with those noted in the 1987 Followup Report, and the Serum Dioxin Analysis Report.

In the 1987 examinations, the mean WBC and platelet counts and the erythrocyte sedimentation rates (ESR) were higher in Ranch Hands than in Comparisons, raising the possibility of a subclinical inflammatory response associated with prior dioxin exposure. In the current study, no group differences were noted in either the WBC or, as reported in Chapter 9, General Health, the ESR. Furthermore, in the current study, current serum dioxin was inversely related to the prevalence of abnormally elevated WBC counts.

Dependent variable-covariate associations confirmed numerous observations that have been well established in clinical practice. In cigarette smokers, cellular hypoxia related to carboxyhemoglobin formation and systemic arterial desaturation in obstructive airway disease combine to raise the hemoglobin and hematocrit in comparison to non-smokers. The increased incidence of chronic bronchitis in smokers is often associated with an elevation in the total WBC count. Older participants were found to have statistically significant reductions in the total RBC count, hemoglobin, and hematocrit, associations that may reflect the increased incidence of chronic disease associated with age.

Race-related associations also were noted. When compared to non-Black participants, Black participants had statistically significant reductions in the RBC indices, findings that may relate to the increased incidence of glucose-6-phosphate dehydrogenase (G-6-PD) deficiency and of hemoglobin variants (S and C) associated with heterozygous sickling disorders. Blacks were found to have a greater prevalence of abnormally low WBC counts than non-Blacks (13.0% versus 3.1%), though the difference in the means (6,580/mm^3 vs. 7,430/mm^3) is not likely of clinical significance.

The longitudinal analyses documented a gradual reduction in the total platelet count in each cohort and across all occupational strata. As in the 1987 followup report, Ranch Hands continue to have a greater reduction in the total platelet count over time than do Comparisons, although the current means (250,700/mm^3 vs. 244,900/mm^3) are nearly equal.

In summary, the results of the current study reveal no evidence for any hematopoietic toxicity associated with prior dioxin exposure. Based on the analyses of three indices noted above (WBC, ESR, and total platelet count), there is no longer evidence that a subclinical inflammatory reaction may be present in Ranch Hands.

SUMMARY

The assessment of the hematologic system comprised analyses on 13 dependent laboratory endpoints. Associations with group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and current dioxin (Models 4, 5, and 6) were examined for each variable. Continuous and discrete analyses were performed for each cell count variable as well as for prothrombin time. In addition, due to the large number of nonzero measurements for absolute neutrophils (bands), absolute eosinophils, and absolute basophils, investigations on these variables incorporated two analyses. First, a discrete analysis was executed on the proportion of zero measurements and secondly, a continuous analysis was performed on the nonzero measurements. Summarized results from the analyses are presented in Tables 16-24 through 16-27. Significant group-by-covariate and dioxin-by-covariate interactions found in the six exposure analyses are listed in Table 16-28.

Model 1: Group Analysis

Analyses on the hematologic cell count variables disclosed significant group effects for platelet count only. Mean platelet count levels were significantly greater for Ranch Hands than for Comparisons in the enlisted flyer and enlisted groundcrew strata of the unadjusted analysis and in the overall, enlisted flyer, and enlisted groundcrew strata of the adjusted analysis. In the unadjusted and adjusted RBC count analyses of all participants, Ranch Hands possessed a marginally significantly greater percentage of abnormally low levels of RBC count than did Comparisons. Analysis restricted to officers detected a marginally greater percentage of abnormally high hemoglobin levels in Ranch Hands than in Comparisons. In the group analyses of the cell count variables, several group-by-covariate interactions were retained, most of which involved one of the smoking risk factors.

Few significant results were observed in the group analyses of the absolute blood count variables. In the adjusted analysis of enlisted flyers, the difference between Ranch Hands and Comparisons in mean levels of nonzero absolute neutrophil (bands) and absolute basophil measurements were significant and marginally significant respectively, with Ranch Hands having a lower mean than Comparisons. Also, the proportion of nonzero measurements for absolute eosinophils was significantly greater for Comparisons than for Ranch Hands for all participants and within the officer category.

Means and abnormality percentages for the remaining hematology variables, prothrombin time, and RBC morphology did not differ significantly between Ranch Hands and Comparisons.

Table 16-24.
Summary of Group Analyses (Model 1) for Hematology Variables
(Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Laboratory				
Red Blood Cell (RBC) Count (C)	ns	ns	ns	ns
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS*	NS	NS	NS
Abnormal High vs. Normal	ns	ns	ns	NS
White Blood Cell (WBC) Count (C)	NS	NS	NS	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	NS	NS	NS	NS
Hemoglobin (C)	NS	NS	ns	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	ns	NS	NS
Abnormal High vs. Normal	NS	NS	NS	NS
Hematocrit (C)	NS	NS	ns	ns
Hematocrit (D)	NS	ns	NS	NS
Platelet Count (C)	NS	ns	+0.016	+0.011
Platelet Count (D)	NS	ns	NS	NS
Prothrombin Time (C)	NS	NS	NS	ns
Prothrombin Time (D)	NS	NS	NS	NS
RBC Morphology (D)	ns	NS	NS	ns
Absolute Neutrophils (segs) (C)	NS	NS	ns	NS
Absolute Neutrophils (bands) (Zero vs. Nonzero) (D)	NS	NS	ns	NS
Absolute Neutrophils (bands) (Nonzero Measurements) (C)	NS	NS	ns	NS
Absolute Lymphocytes (C)	ns	ns	ns	NS
Absolute Monocytes (C)	NS	NS	ns	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	-0.050	-0.018	ns	NS
Absolute Eosinophils (Nonzero Measurements) (C)	ns	ns	ns	NS
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns	ns	NS
Absolute Basophils (Nonzero Measurements) (C)	NS	NS	ns	NS

C: Continuous analysis.
D: Discrete analysis.
+: Difference of means nonnegative.
-: Relative risk < 1.00.
NS or ns: Not significant ($p > 0.10$).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 16-24. (Continued)
Summary of Group Analyses (Model 1) for Hematology Variables
(Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Laboratory				
Red Blood Cell (RBC) Count (C)	****	****	****	****
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS*	NS	NS	NS
Abnormal High vs. Normal	ns	ns	ns	NS
White Blood Cell (WBC) Count (C)	**(NS)	**(NS)	**(ns)	**(NS)
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	NS	ns	NS	NS
Abnormal High vs. Normal	NS	NS	ns	NS
Hemoglobin (C)	**(ns)	**(NS)	**(ns)	**(ns)
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	ns	NS	NS
Abnormal High vs. Normal	NS	NS*	NS	ns
Hematocrit (C)	**(ns)	**(NS)	**(ns)	**(ns)
Hematocrit (D)	NS	ns	NS	NS
Platelet Count (C)	**(+0.036)	ns	+0.014	+0.010
Platelet Count (D)	NS	ns	NS	NS
Prothrombin Time (C)	NS	NS	NS	ns
Prothrombin Time (D)	NS	NS	NS	NS
RBC Morphology (D)	ns	ns	NS	ns
Absolute Neutrophils (segs) (C)	NS	NS	ns	NS
Absolute Neutrophils (bands) (Zero vs. Nonzero) (D)	NS	NS	ns	NS
Absolute Neutrophils (bands) (Nonzero Measurements) (C)	ns	NS	-0.038	NS
Absolute Lymphocytes (C)	ns	ns	ns	NS
Absolute Monocytes (C)	**(NS)	**(NS)	**(ns)	**(NS)
Absolute Eosinophils (Zero vs. Nonzero) (D)	-0.050	-0.018	ns	NS
Absolute Eosinophils (Nonzero Measurements) (C)	ns	ns	ns	NS
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns	ns	NS
Absolute Basophils (Nonzero Measurements) (C)	NS	NS	ns*	NS

C: Continuous analysis.
D: Discrete analysis.
+: Difference of means nonnegative.
-: Relative risk < 1.00.
NS or ns: Not significant ($p > 0.10$).
NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS) or **(ns): Group-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix L-2 for further analysis of this interaction.
**(+0.036): Group-by-covariate interaction ($0.01 < p \leq 0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix L-2 for further analysis of this interaction.
**** Group-by-covariate interaction ($p \leq 0.01$); refer to Appendix L-2 for further analysis of this interaction.
Note: A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 16-25.
Summary of Initial Dioxin Analyses (Model 2) for Hematology Variables
(Ranch Hands Only)

Variable	Unadjusted	Adjusted
Laboratory		
Red Blood Cell (RBC) Count (C)	NS	NS
Red Blood Cell (RBC) Count (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	NS	NS
White Blood Cell (WBC) Count (C)	NS*	**(NS)
White Blood Cell (WBC) Count (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	ns	ns
Hemoglobin (C)	+0.029	NS
Hemoglobin (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	NS	NS
Hematocrit (C)	+0.015	NS*
Hematocrit (D)	NS	NS
Platelet Count (C)	+0.025	NS
Platelet Count (D)	NS	NS
Prothrombin Time (C)	NS	**(+0.019)
Prothrombin Time (D)	ns	ns
RBC Morphology (D)	ns	NS
Absolute Neutrophils (segs) (C)	NS	**(NS)
Absolute Neutrophils (bands) (Zero vs. Nonzero) (D)	ns	**(ns)
Absolute Neutrophils (Nonzero Measurements) (bands) (C)	NS	**(ns)
Absolute Lymphocytes (C)	NS	NS
Absolute Monocytes (C)	NS*	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	NS	**(NS)
Absolute Eosinophils (Nonzero Measurements) (C)	NS	ns
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	+0.037	NS*

C: Continuous analysis.
D: Discrete analysis.
+: Slope nonnegative.
NS or ns: Not significant ($p > 0.10$).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS) or **(ns): Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix L-2 for further analysis of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 16-26.
Summary of Categorized Dioxin Analyses (Model 3) for Hematology Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Laboratory				
Red Blood Cell (RBC) Count (C)	ns	ns	ns	ns
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	+0.049	NS*	ns	NS
Abnormal High vs. Normal	ns	NS	ns	ns
White Blood Cell (WBC) Count (C)	ns	NS	NS*	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	ns	NS	NS	NS
Abnormal High vs. Normal	NS	NS	NS	NS
Hemoglobin (C)	NS	ns	NS	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	NS	ns	NS
Abnormal High vs. Normal	NS	NS	NS	NS
Hematocrit (C)	NS	ns*	NS	ns
Hematocrit (D)	NS*	NS	NS	NS
Platelet Count (C)	ns	NS	+<0.001	+0.004
Platelet Count (D)	ns	ns	+0.027	NS
Prothrombin Time (C)	NS	ns	ns	ns
Prothrombin Time (D)	NS	NS	ns	NS
RBC Morphology (D)	ns	ns	ns	ns
Absolute Neutrophils (segs) (C)	ns	ns	NS*	NS
Absolute Neutrophils (bands) (Zero vs. Nonzero) (D)	NS	NS	ns	NS
Absolute Neutrophils (bands) (Nonzero Measurements) (C)	NS	NS	ns	ns
Absolute Lymphocytes (C)	ns	ns	NS	NS
Absolute Monocytes (C)	NS	ns	NS*	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	ns	ns	ns	ns
Absolute Eosinophils (Nonzero Measurements) (C)	NS	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	NS	ns	NS	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk $\geq$ 1.00 for discrete analysis or difference of means nonnegative for continuous analysis.
NS or ns: Not significant ($p > 0.10$).
NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 16-26. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Hematology Variables (Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Laboratory				
Red Blood Cell (RBC) Count (C)	**(ns)	**(ns)	**(ns*)	**(ns*)
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS*	NS	ns	NS
Abnormal High vs. Normal	ns	ns	ns	ns
White Blood Cell (WBC) Count (C)	NS	NS	NS	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	NS	NS	NS	NS
Abnormal High vs. Normal	NS	NS	ns	NS
Hemoglobin (C)	**(NS)	**(ns)	**(NS)	**(ns)
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	NS	ns	NS
Abnormal High vs. Normal	NS	NS	NS	NS
Hematocrit (C)	**(NS)	**(ns)	**(NS)	**(ns)
Hematocrit (D)	NS	NS	NS	NS
Platelet Count (C)	NS	NS	+<0.001	+0.010
Platelet Count (D)	ns	ns	+0.029	NS
Prothrombin Time (C)	**(NS)	**(ns)	**(ns)	**(ns)
Prothrombin Time (D)	NS	NS	NS	NS
RBC Morphology (D)	-0.049	ns	NS	ns
Absolute Neutrophils (segs) (C)	ns	NS	NS	NS
Absolute Neutrophils (bands) (Zero vs. Nonzero) (D)	****	****	****	****
Absolute Neutrophils (bands) (Nonzero Measurements) (C)	ns	NS	ns	NS
Absolute Lymphocytes (C)	NS	ns	ns	ns
Absolute Monocytes (C)	NS	ns	NS*	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	ns	ns	ns	ns
Absolute Eosinophils (Nonzero Measurements) (C)	NS	ns	ns	ns*
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	NS	ns	NS	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis or difference of means nonnegative for continuous analysis.
-: Difference of means negative.
NS or ns: Not significant ($p > 0.10$).
NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS) or **(ns): Categorized dioxin-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix L-2 for further analysis of this interaction.
**(ns*): Categorized dioxin-by-covariate interaction ($p \leq 0.05$); marginally significant when interaction is deleted; refer to Appendix L-2 for further analysis of this interaction.
**** Categorized dioxin-by-covariate interaction ($p \leq 0.01$); refer to Appendix L-2 for further analysis of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 16-27.
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Hematology Variables (Ranch Hands Only)

Variable	UNADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Laboratory			
Red Blood Cell (RBC) Count (C)	NS*	+0.042	NS
Red Blood Cell (RBC) Count (D)			
Abnormal Low vs. Normal	ns	ns	ns
Abnormal High vs. Normal	NS	NS	NS
White Blood Cell (WBC) Count (C)	NS	NS	NS
White Blood Cell (WBC) Count (D)			
Abnormal Low vs. Normal	NS	NS	NS
Abnormal High vs. Normal	ns	ns	ns
Hemoglobin (C)	NS	NS	NS
Hemoglobin (D)			
Abnormal Low vs. Normal	ns	ns	ns
Abnormal High vs. Normal	NS	NS	NS
Hematocrit (C)	NS	NS	NS
Hematocrit (D)	NS	NS	NS
Platelet Count (C)	+0.033	+0.018	+0.045
Platelet Count (D)	+0.014	+0.017	+0.016
Prothrombin Time (C)	ns	ns	NS
Prothrombin Time (D)	ns	ns	ns
RBC Morphology (D)	NS	NS	NS
Absolute Neutrophils (segs) (C)	NS	NS	NS
Absolute Neutrophils (bands) (Zero vs. Nonzero) (D)	NS	NS	NS
Absolute Neutrophils (bands) (Nonzero Measurements) (C)	ns	ns	ns
Absolute Lymphocytes (C)	NS	NS	NS
Absolute Monocytes (C)	NS	NS	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	NS	NS*	NS
Absolute Eosinophils (Nonzero Measurements) (C)	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	NS	NS	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk $\geq$ 1.00 for discrete analysis or slope nonnegative for continuous analysis.
NS or ns: Not significant ($p > 0.10$).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 16-27. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Hematology Variables (Ranch Hands Only)

Variable	ADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Laboratory			
Red Blood Cell (RBC) Count (C)	NS	NS*	NS
Red Blood Cell (RBC) Count (D)			
Abnormal Low vs. Normal	ns	ns	ns
Abnormal High vs. Normal	NS	NS	NS
White Blood Cell (WBC) Count (C)	**(NS)	**(NS)	**(ns)
White Blood Cell (WBC) Count (D)			
Abnormal Low vs. Normal	**(NS)	**(NS)	**(NS)
Abnormal High vs. Normal	**(-0.029)	**(ns*)	**(-0.034)
Hemoglobin (C)	NS	NS	NS
Hemoglobin (D)			
Abnormal Low vs. Normal	ns	ns	ns
Abnormal High vs. Normal	NS	NS	NS
Hematocrit (C)	NS	NS	NS
Hematocrit (D)	NS	NS	NS
Platelet Count (C)	ns	NS	ns
Platelet Count (D)	+0.014	NS*	ns
Prothrombin Time (C)	NS	ns	NS
Prothrombin Time (D)	**(ns)	ns	ns
RBC Morphology (D)	NS*	NS*	+0.045
Absolute Neutrophils (segs) (C)	**(NS)	**(NS)	**(NS)
Absolute Neutrophils (bands) (Zero vs. Nonzero) (D)	****	****	****
Absolute Neutrophils (bands) (Nonzero Measurements) (C)	NS	NS	ns
Absolute Lymphocytes (C)	ns	ns	ns
Absolute Monocytes (C)	NS	NS	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	NS*	NS*	**(NS)
Absolute Eosinophils (Nonzero Measurements) (C)	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	ns	**(NS)	**(ns)

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
-: Relative risk < 1.00.
NS or ns: Not significant ($p > 0.10$).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS) or **(ns): Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix L-2 for further analysis of this interaction.
**(ns*): Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); marginally significant when interaction is deleted; refer to Appendix L-2 for further analysis of this interaction.
**** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); refer to Appendix L-2 for a detailed description of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or a nonnegative slope for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 16-28.
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Hematology Variables

Model	Variable	Covariate
1[a]	Red Blood Cell (RBC) Count (C)	Current Cigarette Smoking
	White Blood Cell (WBC) Count (C)	Race
	Hemoglobin (C)	Current Cigarette Smoking, Lifetime Cigarette Smoking History
	Hematocrit (C)	Current Cigarette Smoking, Lifetime Cigarette Smoking History
	Platelet Count (C)	Occupation
	Absolute Monocytes (C)	Race
2[b]	White Blood Cell (WBC) Count (C)	Race, Occupation
	Absolute Neutrophils (segs) (C)	Race
	Absolute Neutrophils (bands) (C)	Lifetime Cigarette Smoking History
	Absolute Neutrophils (bands) (C)	Occupation
	Absolute Eosinophils (C)	Age, Occupation
3[c]	Red Blood Cell (RBC) Count (C)	Current Cigarette Smoking
	Hemoglobin (C)	Current Cigarette Smoking, Lifetime Cigarette Smoking History
	Hematocrit (C)	Current Cigarette Smoking, Lifetime Cigarette Smoking History
	Prothrombin Time (C)	Age
	Absolute Neutrophils (bands) (C)	Lifetime Cigarette Smoking History
4[d]	White Blood Cell (WBC) Count (C)	Race
	White Blood Cell (WBC) Count (D)	Race
	Prothrombin Time (D)	Lifetime Cigarette Smoking History
	Absolute Neutrophils (segs) (C)	Race
	Absolute Neutrophils (bands) (C)	Lifetime Cigarette Smoking History
5[e]	White Blood Cell (WBC) Count (C)	Race
	White Blood Cell (WBC) Count (D)	Race
	Absolute Neutrophils (segs) (C)	Race
	Absolute Neutrophils (bands) (C)	Lifetime Cigarette Smoking History
	Absolute Basophils (C)	Race
6[f]	White Blood Cell (WBC) Count (C)	Race
	White Blood Cell (WBC) Count (D)	Race
	Absolute Neutrophils (segs) (C)	Race
	Absolute Neutrophils (bands) (C)	Lifetime Cigarette Smoking History
	Absolute Eosinophils (C)	Occupation
	Absolute Basophils (C)	Race

C: Continuous Analysis
D: Discrete Analysis
[a] Group Analysis (Ranch Hands vs. Comparison).
[b] Ranch Hands—Log_2 (Initial Dioxin).
[c] Categorized Dioxin.
[d] Ranch Hands—Log_2 (Current Lipid-Adjusted Dioxin + 1).
[e] Ranch Hands—Log_2 (Current Whole-Weight Dioxin + 1).
[f] Ranch Hands—Log_2 (Current Whole-Weight Dioxin + 1), Adjusted for Total Lipids.

Model 2: Initial Dioxin Analysis

In the unadjusted analysis of the cell count variables, hemoglobin, hematocrit, and platelet count displayed significant associations with initial dioxin, which indicated a positive dose-response relationship. However, adjustment for covariate information caused the dioxin effect for both platelet count and hemoglobin to become nonsignificant. Adjusted analysis results for hematocrit became marginally significant. Analyses on the remaining cell count endpoints disclosed nonsignificant associations with initial dioxin.

Nonzero measurements of absolute basophils increased significantly with initial dioxin in the unadjusted Model 2 analyses; the adjusted slope was only marginally significant. A marginally significant positive association between initial dioxin and absolute monocytes was found in the unadjusted analysis.

Analyses on the remaining hematology variables detected a significant positive relationship between continuously measured prothrombin time and initial dioxin in the adjusted analysis.

Model 3: Categorized Dioxin Analysis

Significant results from the categorized dioxin analyses of the cell count variables were seen mainly in the analyses of platelet count. Measured continuously, mean levels of platelet count in the high and low plus high Ranch Hand categories were significantly greater than those of the Comparisons in both the unadjusted and adjusted analyses. Additionally, the percentage of abnormally high platelet count levels was greater in high Ranch Hands than Comparisons. Adjusted RBC count means displayed marginally significant inverse associations in the analyses of high Ranch Hands and low plus high Ranch Hands versus Comparisons. The inverse associations indicate that mean levels of RBC count in the aforementioned Ranch Hand categories were lower than the mean levels of RBC count in the Comparison group. Analyzed discretely, the percentage of abnormally low RBC counts in background Ranch Hands was significantly greater than that of the Comparisons in the unadjusted analysis and marginally significant in the adjusted analysis. Several cell count variables displayed marginally significant associations with categorized dioxin in the unadjusted analyses that became nonsignificant after covariate adjustment (i.e., abnormal low RBC counts, continuously measured WBC counts, continuously measured hematocrit, and abnormal low hematocrit levels).

Only marginally significant results were disclosed in the categorized dioxin analyses of the absolute blood count variables. Unadjusted means for absolute neutrophils (segs) and absolute monocytes were greater in high Ranch Hands than Comparisons. However, this result remained marginally significant only for absolute monocytes after covariate adjustment. Adjusted mean levels of nonzero absolute eosinophil measurements were lower in the low plus high Ranch Hand category than in the Comparison group.

In the adjusted analysis of coagulation, the percentage of abnormal RBC morphology measurements was significantly lower in the background Ranch Hand category than in the Comparison group.

Models 4, 5, and 6: Current Dioxin Analyses

Current dioxin analyses of platelet count, similar to the other exposure analyses, led to significant results. Unadjusted for covariates, platelet counts in both discrete and continuous forms were positively associated with each of the current dioxin measurements. However, with the exception of significant and marginally significant associations between discrete platelet counts and current dioxin in Models 4 and 5, the adjusted results became nonsignificant. Adjusted relative risks of abnormally high WBC counts were significantly less than 1.00 in the adjusted analyses of Models 4 and 6. The adjusted relative risk was marginally significant in Model 5. Marginally significant and significant positive associations between RBC counts and current dioxin were found in the unadjusted analyses of Models 4 and 5. Adjusted results of RBC counts became nonsignificant in Model 4 and marginally significant in Model 5.

Marginally significant positive associations between the proportion of zero measurements of absolute eosinophils and current dioxin were found in the unadjusted analysis of Model 5 and the adjusted analyses of Models 4 and 5. Current dioxin analyses on the remaining absolute blood count variables were nonsignificant. Dioxin-by-covariate interactions retained in the adjusted analyses primarily involved either race or lifetime cigarette smoking history.

Among the remaining hematology variables, RBC morphology was significantly related to whole-weight current dioxin adjusted for total lipids in the adjusted analysis of Model 6. Positive relationships of marginal significance also were observed in the lipid-adjusted and whole-weight current dioxin analyses of RBC morphology.

CONCLUSION

The thirteen endpoints analyzed in the hematology assessment provide a comprehensive evaluation of the three peripheral blood lines (erythrocytes, leukocytes, and platelets) and their relation to dioxin exposure. In the analyses of these variables, only platelet count exhibited significant associations with the herbicide exposure indices. Ranch Hands in the enlisted flyer and enlisted groundcrew categories possessed statistically significant higher mean platelet counts than Comparisons, although the result cannot be considered significant from a clinical point of view. Analyses employing extrapolated levels of initial dioxin showed that Ranch Hands with high dioxin levels had significantly greater mean platelet count measurements than Comparisons. Platelet counts also were positively associated with current serum dioxin measurements, although the association became nonsignificant when adjusted for covariates. These results support the results found in both the 1987 followup study and in the serum dioxin analysis of the 1987 followup study, but the biologic significance is uncertain.

Results from the 1987 followup study generated questions regarding the possibility of a subclinical inflammatory response associated with prior dioxin exposure. This was due to elevated WBC counts, platelet counts, and erythrocyte sedimentation rates in Ranch Hands. However, the current study did not produce significant results to support this possibility. Therefore, in conclusion, there is no evidence from the present study that suggests an association between hematopoietic toxicity and prior dioxin exposure.

CHAPTER 16
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